U.PORTO

INSTITUTO DE CIÊNCIAS BIOMÉDICAS ABEL SALAZAR
UNIVERSIDADE DO PORTO

EFFECT OF ACUPUNCTURE ON PAIN INTENSITY AND GRIP STRENGTH IN SYMPTOMATIC RHIZARTHROSIS

PROSPECTIVE,RANDOMIZED, NON-BLINDED CLINICAL STUDY WITH WAITINGLIST DESIGN

Christiane Grünecker

Dissertação de Mestrado em Medicina Tradicional Chinesa

2014

Christiane Grünecker

EFFECT OF ACUPUNCTURE ON PAIN INTENSITY AND GRIP STRENGTH IN SYMPTOMATIC RHIZARTHROSIS

PROSPECTIVE,RANDOMIZED, NON-BLINDED CLINICAL STUDY WITH WAITINGLIST DESIGN

Dissertação de Candidatura ao grau de Mestre em Medicina Tradicional Chinesa submetida ao Instituto de Ciências Biomédicas Abel Salazar da Universidade do Porto
Orientador – Dr. Henry Johannes Greten
Categoria – Professor Asscociado convidado
Filiação – Heidelberg School of Chinese Medicine
Instituto Ciências Biomédicas Abel Salazar da Universidade do Porto

DEDICATION

To my wonderful husband Walter
and to my sensational family
Benjamin, Daniel, Joana, Lia, Nika
Josua, Jeanne, Jaelle, Ilian, Johannes, Lisa
and Tiger

Acknowlegdement

I would like to thank :

Prof. Greten for being an inspiring and motivating scientist

Dr. Nuno Correia for being a hero

Prof. Jorge Machado for keeping up the fight for TCM

MSc. Maria Joao Santos for being a wonderful professor

Dra. Petra Fröschen for always being on top of things organisation-wise

Andrea Braun-Radnedge for successfully juggling with the technical aspects

Dipl. Ing. August Grünecker for having been a person of excellence

Abbreviations

ALT	Algor Laedens Theorie
DASH	Disabilities of the Arm, Shoulder and Hand Questionnaire
OA	Osteoarthrosis
TCM	Traditional Chinese Medicine
VAS	Visual Analogue Scala
TCM	Traditional Chinese Medicine
TMCjoint	Trapeziometacarpal (joint)
P	Pulmo
IC	Intestinum crassum

Index

1. **BASIC KNOWLEDGE**

1.1 Functional anatomy of the trapeziometacarpal joint 21

1.1.1 Common problems of the trapeziometacarpal joint 22

1.1.1.1 Rhizarthrosis : Arthrosis of the trapeziometacarpal joint 22

1.1.1.2 Pathophysiology of Rhizarthrosis 24

1.1.1.3 Conservative Treatment of Rhizarthrosis 24

1.1.1.4 Indications for surgical intervention in rhizarthrosis 25

1.2 **History of acupuncture** 26

1.2.1 Three important concepts in acupuncture 29

1.2.1.1 The Qi 29

1.2.1.2 Yin and Yang 29

1.2.1.3 The Five Elements 29

1.2.2 The Heidelberg Model of Traditional Chinese Medicine 32

1.2.2.1 The guiding criteria : four different physiological levels 33

1.2.2.2 The orbes: physiological patterns 34

1.2.2.3 Sinusoidal-pattern of phases 35

1.2.3 Analogies of the phases with neurohormonal mechanisms 37

1.2.4 Diagnosis according to the Heidelberg Model of TCM 38

1.2.4.1 Constitution 38

1.2.4.2 Agent 39

1.2.4.3 The Orbes 40

1.2.4.4 Guiding-criteria (GC) 41

1.2.4.5 The Algor Laedens Theory (“harmful cold disease”) = ALT 43

1.2.4.5.1 The three Yang/ Extimal Stages 43

1.2.4.5.2 The three Yin/ Intimal Stages 44

1.2.4.6 Four kinds of mechanisms may cause disease 46

1.2.4.7 Pain according to Heidelberg model of Traditional Chinese Medicine 46

1.2.4.8 Bi-Syndrome 50

1.2.4.8.1 TCM treatment concept for osteoarthrosis 53

1.2.4.8.2 The scientific evidence base of Chinese medicine in OA treatment 56

1.2.4.8.3 Conclusion 56

1.2.5 Generalities of acupuncture research 56

1.2.5.1 General proposed mechanisms of action of acupuncture 56

1.2.5.1.1 Endorphins 57

IX

1.2.5.1.2 Functional MRI 57
1.2.5.1.3 Connective tissue and mast-cell degranulation 57
1.2.5.1.4 Acupuncture clinical application 57
1.2.5.1.5 Acupuncture-related adverse events 58
1.2.5.2 Challenges in acupuncture research: the issue of good control, placebo effect, and point specificity 59
1.2.5.3 Acupuncture's stimulation modality: manual versus electroacupuncture 62

2 **CLINICAL RESEARCH PROTOCOL** 67
2.1 Academic and medical background 67
2.2 Background 67
2.2.1 Study-Focus Rhizarthrosis 67
2.3 Justification of the study 68
2.4 Research team 69
2.4.1 Main investigators 69
2.4.2 Research supervisors 69
2.5 Study hypothesis 69
2.6 Methods 70
2.6.1 Study population 70
2.6.2 Study design 70
2.6.3 Randomization to intervention groups 70
2.6.4 Outcomes and measurements 70
2.6.4.1 Main outcomes 70
2.6.4.2 Secondary Outcomes 71
2.6.5 Eligibility criteria 71
2.6.6 Sampling and recruitment procedures 71
2.6.7 Experimental procedures 71
2.6.7.1 Intervention 73
2.6.7.2 Measurements 74
2.6.8 Statistical plan 74
2.6.9 Financial Issues 74
2.6.10 Ethical considerations 74
2.6.11 Expected results 75

3 **RESULTS** 78

3.1 Conclusion 82

Index of Figures

Figure 1. Illustration of the trapeziometacarpal joint (TMJ) of the left thumb 21
Figure 2. Stages I – IV of rhizarthrosis 23
Figure 3. The Theodicee, the main work of Leibniz 28
Figure 4.Pseudo Philosophy of TCM (Greten 2008) 31
Figure 5. The Taiji sign 33
Figure 6. The Heidelberg Model of TCM 33
Figure 7. Regulation as a technical process 35
Figure 8. fou qi emblem 36
Figure 9. Vegetative activity 37
Figure 10. Schematic representation of the TCM methodology of diagnosis 38
Figure 11. ALT related orbs and cross-linked orbs 45
Figure 12. The Martin Vigorimeter 70
Figure 13. Schematic representation of the experiment set-up 73
Figure 14. Initial differences between intervention group and waiting group 78
Figure 15. Study results – Intervention group - improvement 79
Figure 16. Study results – Waiting list group – improvement 79
Figure 17. Study results – Intervention group - evolution 80
Figure 18. Study results – Waiting list group - evolution 80
Figure 19. Study results – Follow-up group – improvement baseline vs 4 weeks 81
Figure 20. Study results – Follow-up group – improvement 2 weeks vs 4 weeks 81
Figure 21. Study results – improvements between groups – baseline vs 2 weeks 82

Index of Tables

Table 1. Summary of treatment of capsular disorders 25
Table 2. Five Element Theory Chart 30
Table 3. Four levels of regulation 34
Table 4. The agents 40
Table 5. Guiding criteria 42

Abstract

Effect of Acupuncture on Pain Intensity and Grip Strength in Symptomatic Rhizarthrosis: a clinical research protocol.

Christiane Grünecker[1], Nuno Correia[2,4], Henry Greten[3,5]

(1) TCM Master Programme, Abel Salazar Institute for Biomedical Sciences; Physiotherapy Department, Viana do Castelo Private Hospital, Portugal, (2) Acupuncture Clinic, Alfena Private Hospital, Portugal; (3) Abel Salazar Institute for Biomedical Sciences, University Porto, Portugal; (4) Internal Medicine, Emergency Department, Hospital Center São João, Porto, Portugal; (5) Heidelberg School of Chinese Medicine

Introduction:

Osteoarthrosis of the Trapeziometacarpaljoint or Rhizarthrosis:
Occurs most frequently in middle-aged or postmenopausal women and affects at least 1 in 3 women over 65 and a quarter of men over 75. Rhizarthrosis is often bilateral .

Etiology: Still very unclear. There is evidence that ligament laxity and trapeziometacarpal subluxation are important early events in the development of thumb arthrosis.

Main Symptoms: Pain in the dorsoradial and thenar area of the hand and a loss of manual ability and grip strength.

Great functional importance of the trapezometacarpaljoint explains that any pathological process that troubles its funcionality could lead to chronic social and occupational disability and have significant repercussions on everyday activity.

Objective:
To study the effect of suppletive acupuncture on pain intensity and grip strenght in symptomatik rhizarthrosis including a evaluation of its ongoing effect in the two weeks following end of intervention

Methods:

Ethics approval: The research protocol was approved by the Ethics Committee of the

University of Porto. PROJETO Nº 073/2014

Study design:
Prospective, randomized, non-blinded clinical study, with waitinglist-control

Sample:
n= 38 adults

Inclusion criteria:

diagnosis of rhizartrosis ,Eaton Stage < 3;

age over 18 y.o, no surgery, no steroidinjection,

no change of medication during the study; informed consent.

Exclusion criteria:

Rhizarthrosis Eaton Stage =/>3

rheumatologic diseases,

anticoagulant treatment

glucocorticoids, immunosuppressives;

intra-articular injection or steroid injection in the 3 months before study.

Interventiongroup

n=38 (33 female), 46-75 y.o.,

randomly selected for Interventiongroup

submitted to acupuncture, 4 sessions in 2 weeks,

assessed before and after acupuncture.

Waiting list Control group
n= 15 (13 female) control group , 46-75 y.o.,
randomly selected for waiting list, stood there for two weeks, were assessed before and after this two weeks while standing by with no other treatment.

Follow-up group :

In order to get an idea of the washout phase of suppletive acupuncture and its possible further evolution of symptoms, we extended the scope of the trial by one more serie of measurements two weeks after completion of treatments .

A group of n=12 patients (10 female), aged from 46 years to 75 years,

were recruited from the original Experimentalgroup

Only the parameters VAS and Grip Strength were taken into account.

Intervention:

Patients were treated with classical suppletive acupuncture in a sequence of four treatments in two weeks.

The selection of acupuncture points was based on potential local and segmental effects and followed the "the Heidelberg Model of Traditional ChineseMedicine"

Manual acupuncture was performed with rotation of the needles

until a sensation of numbness („DeQi“) was attended.

Than needles remaind for 20 minutes

Experimentalgroup was subject to four treatments in two weeks

Measurements:

Before and after the treatments, measurements were made by:

DASH (Disability of Arm, Shoulder and Hand),

VAS (visual analog scale) and

GRIP STRENGHT (evaluation by means of a Martin vigorimeter).

Results:

Review of the recent literature indicates that acupuncture has effects on pain relief for different osteoarthrotic diseases and its analgesic mechanisms are well studied.

In the proposed study, patients of Intervention group experienced a improvement in DASH 44,51%, Pain intensity improved in 40,54 %, Grip strength improved 19,21 %

The Follow-up group showed an improvement of VAS of 52, 85% in total and Grip Strength had and improvement of 16,62% (after four weeks....two weeks intervention and two weeks followup without any intervention)

In the waiting-list group the difference was: 1,67 % increase in VAS, 1,18% reduction in Grip Strength and 1,25 increase % in Dash.

Discussion/Conclusion:

We found no reliable published studies on acupuncture for Rhizarthrosis (Ostoearthrosis

of the Trapeziometacarpaljoint).
Given the biological plausibility of acupuncture's effects and its clinical good outcomes already shown for other pathologies, it may be possible that acupuncture also has benificial effects on Rhizarthrosis.
The study suggests:

A:
The results from the proposed prospective clinical study suggest that the effects of the chosen acupuncture points may be associated with a therapeutic benefit in the pathology of Rhizarthrosis

However, controversy persists whether the observed effects are specific to acupuncture or merely nonspecific consequences of needling.
Therefore, a future study could have the objective to determine the efficacy of different acupuncture treatment modalities. There could be compared verum and sham acupuncture (needling of non-specific points) in a prospective randomised trial with a double-blinded study design.
If acupuncture shows good results it may then be an additional therapeutic tool for the multidisciplinary treatment of this common disease.

B:
The technique of suppletive needling seems to have a longer period of effect than expected.
In order to avoid a carry-over effect in a future possible clinical study with cross-over design, we suggest further studies with exact mesurement of the wash-out phase after suppletive needling.

Keywords
Traditional Chinese Medicine, acupuncture, Heidelberg Model of TCM, osteoarthrosis, rhizarthrosis, trapeziometacarpal joint, grip strength

CHAPTER ONE

Background Knowledge

1. Basic Knowledge

1.1. Functional anatomy of the trapeziometacarpal joint

The basal joint of the thumb is formed by the articulation between the trapezium bone proximally and the first metacarpal bone distally. It is therefore called the trapeziometacarpal joint or the carpometacarpal joint of the thumb.(Fig. 1) The trapezium, a bone of the second carpal row, articulates with the scaphoid bone proximally, the trapezoid medially and the bases of the first and second metacarpal bones distally. The trapezium is on the palmar and radial side of the wrist. It is angled such that it projects towards the palmar side. It angles the first metacarpal bone (the most proximal bone of the thumb) radially and in a palmar direction. The articular facet of the trapezium with the first metacarpal is angled 35 degrees towards the palmar direction and 20 degrees radially. This results in the neutral position of the thumb being 35 degrees in a palmar direction and 20 degrees in a radial direction [11].

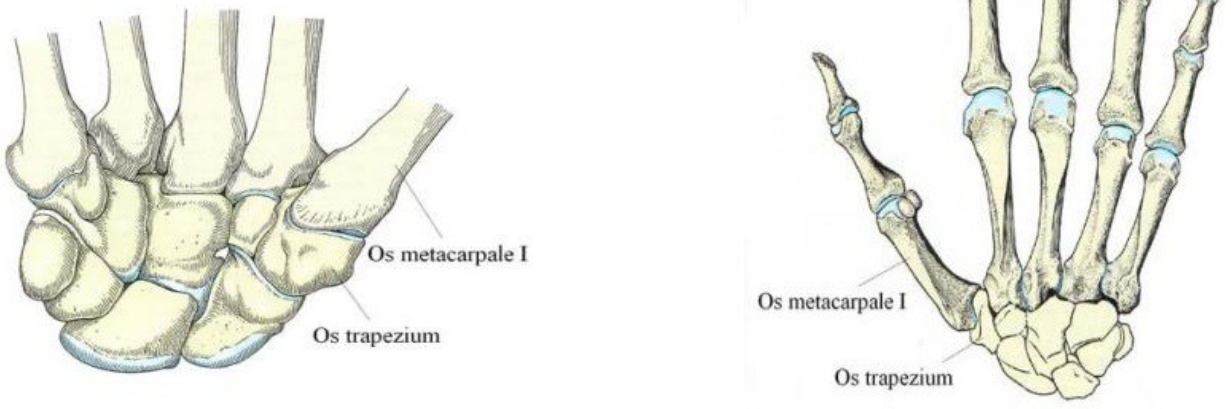


Fig. 1. Illustration of the trapeziometacarpal joint (TMC joint) of the left thumb. The first (M1) and second (M2) metacarpals, the trapezium (T), the trapezoid (TZ), the scaphoid (S) and the capitate (C) bones are illustrated. Illustration courtesy of Mr Donald Sammut, Consultant Hand Surgeon, The Hand Clinic, Windsor.

The trapeziometacarpal joint is a saddle joint with wide mobility due to extensive articular surfaces. It is called a saddle joint because the trapezial articular surface is concave in a

dorsopalmar direction and convex in the radioulnar direction. The first metacarpal base is complimentary to the trapezial articular surface. The trapezium is compared to the saddle of a horse and the base of the first metacarpal bone may be compared to the horse rider as it is mobile. It is a synovial joint and is surrounded by a joint capsule that is strengthened by three ligaments. The most important of these is the ulnar beak ligament. This is a very thick and wide ligament that runs from the crest of the trapezium and attaches to the ulnar side of the base of the first metacarpal. This ligament maintains the stability of the thumb and is tense in abduction of the first metacarpal. The other two ligaments are less widely described as they are believed to be less important in the stability of the thumb. The radial ligament originates from the radial side of the trapezium and travels dorsally and medially to attach to the dorsal tubercle of the first metacarpal. A palmar wide ligament is also sometimes described [11, 12, 8]. A wide range of movement is permitted at the trapeziometacarpal joint: flexion, extension, abduction, adduction, opposition and retroposition.

1.1.1.Common problems of the trapeziometacarpal joint

1.1.1.1.Rhizarthrosis : Arthrosis of the trapeziometacarpal joint

Apart from disorders of the innert structures, rhizarthrosis (RA) is a common, painful and debilitating condition. It is more common in women and most commonly presents in Caucasian women in their late forties [10]. It affects approximately 16-20% of women over 45 years old and 6% of men over this age [1]. It is the site most frequently operated on in the upper extremity for primary osteoarthritis. [7]. Pain is the main presenting symptom. It is often brought on by writing, by opening jars and using the hand for a long time, particularly in pinching movements and there is difficulty in performing these activities. The patients often have weakness due to the pain that may affect their ability to work, perform activities of daily living and follow leisure pursuits. They may also have an adduction deformity of their thumb. Signs include tenderness over the carpometacarpal joint at the base of the thumb,thenar wasting, reduced pinch grip strength and crepitus on moving the thumb [10, 3]. The severity of basal thumb rhizarthrosis can be graded according to the Eaton stages. Eaton Stage I basal thumb rhizarthrosis indicates joint pain and symptoms but no joint space-narrowing or cartilage degeneration shown on X-ray. Eaton stage II is classified as joint space narrowing seen on X-ray with osteophytes present of less than 2mm in size. An osteophyte is a small outgrowth of bone which

occurs at joints in association with degeneration of joint cartilage. Eaton Stage III rhizarthrosis is characterised by osteophytes of greater than 2mm in size being present on x-ray and significant destruction of the joint. Instage IV basal thumb OA there is significant degeneration of the scaphotrapezial joint in addition to the trapeziometacarpal joint [2]. (Fig. 2)

Fig. 2 Stages I – IV of rhizarthrosis

1.1.1.2. Pathophysiology of Rhizarthrosis

Many authors have described theories on how rhizarthrosis of the base of the thumb occurs. There is often degeneration of the ulnar beakligament due to recurrent stress and overuse which leads to ligament and joint instability. With increased laxity there may be abnormal translation of the first metacarpal on the trapezium. This can result in excessive shear forces between the joint surfaces [9, 6, 5]. In addition there is articular degeneration. This may be secondary to instability which leads to joint surface incongruity. The incongruity may result in areas of high contact stress developing in the joint. This then causes cartilage erosion and the symptoms and signs of rhizarthrosis [1]. It has been shown that articular degeneration occurs on the palmar side first and gradually progresses to dorsoradial cartilage degeneration in the later stages of rhizarthrosis of the joint [7, 4]. Radiological studies looking at the angle of the trapezium comparedto the second metacarpal have shown that there is an increased radial trapezial tilt in Eaton stages III and IV compared to Eaton stages I and II rhizarthrosis of the base of the thumb [1, 5]. Studies have also shown accessory tendons of abductor pollicis longus inserting into the radial side of the metacarpal base in some people. These pull the metacarpal base radially and hence have a tendency to cause joint instability and may contribute to the development of rhizarthrosis [12].

1.1.1.3. Conservative Treatment of Rhizarthrosis

The treatment that is chosen depends on the stage of the arthrosis and the functional disability of the joint. Classically, conservative treatment of osteoarthritis of the trapeziometacarpal joint includes analgesics, joint protection, strengthening exercises of the intrinsic and extrinsic muscles of the thumb, and splints.[16] Surgical management is recommended to relieve intractable pain. In early arthrosis, deep transverse friction to the anterior and lateral aspect of the capsule can cause the pain to cease but does not influence mobility. Later in the course of the condition, intra-articular triamcinolone can be tried. It usually has a temporary result only. An open label trial found that steroids had no benefit on carpometacarpal pain at 26 weeks,while a randomized controlled trial evaluating steroids against placebo injection showed that steroids had no benefit in moderate to severe trapeziometacarpal osteoarthritis at 24 weeks.[17] (Table 1)

Summary of treatment of capsular disorders		
Deep friction	**Intra-articular injection**	**Surgery**
–	Rheumatoid arthritis	Rheumatoid arthritis
Traumatic arthritis	Traumatic arthritis	–
Early arthrosis	Moderate arthrosis	Severe arthrosis

Table 1 Summary of treatment of capsular disorders

However, the long-term results of triamcinolone are more effective when a traumatic arthritis has supervened. During the last few decades, intra-articular injections with hyaluronic acid have been promoted as a valuable alternative to intra-articular injections with steroids.[18] A few open label trials [19, 20] found that hyaluronic acid reduced pain and improved grip strength during 6-month follow-up, and two randomized controlled trials stated ‘non-inferiority’ of hyaluronic acid com -pared with steroids for pain relief at 26 weeks.[21, 22]

1.1.1.4. Indications for surgical intervention in rhizarthrosis

If, despite conservative measures, pain or deformity interferes with daily activities such as holding a key or gripping an object, surgical treatment is advocated. As already mentioned, the trapeziometacarpal joint is the most commonly surgically reconstructed joint for osteoarthritis in the upper limb [7, 9]. The first operation which can be considered for early rhizarthrosis is reconstruction of the ulnar beak ligament. This is achieved using a tendon slip from the flexor carpi radialis tendon. As it does not involve any of the articular surfaces, it is reserved for patients with joint laxity without appreciable degenerative changes. Thumb metacarpal osteotomy is another operation which can be effective in early disease. It transfers load bearing from the worn volar cartilage to the more intact dorsal articular surface. As well as giving symptom relief it also slows the progression to more severe osteoarthritis [4]. Another more experimental method of reconfiguring the joint alignment is wedge osteotomy of the trapezium. This realigns the trapezial saddle reducing metacarpal subluxation. However, studies are in their early stages and evidence for this procedure is limited [5]. For more severe disease with significant degenerative changes the surgical options include trapeziectomy, arthrodesis and total joint arthroplasty. Trapeziectomy is associated with good pain relief but can lead

to weakness and instability lasting several months so is often reserved for Eaton Stages III and IV osteoarthritis [5, 3, 10]. Trapeziectomy may be performed in isolation or in combination with tendon sling interposition or ligament reconstruction. However, the outcome of these operations appears to be equivalent [13]. Arthrodesis is a less frequently performed procedure in the trapeziometacarpal joint than other joints in the hand. It is associated with increased joint stability but longer immobilisation and an incidence of non-union [4]. It leaves a strong but rather immobile thumb. Total joint arthroplasty has been a less successfulprocedure in this joint. There is frequent loosening of the components, implant fracture and an increased infection rate. Revision of total joint replacements of this joint are common [14, 10]. The choice of surgical procedure for trapeziometacarpal arthritis is still controversial. There is limited evidence as to which procedure produces optimal results whilst limiting complications. Therefore, randomised clinical trials are awaited comparing these surgical techniques [15].

1.2. History of Acupuncture

Acupunctur is supposed to be one of the oldest medical procedures in the world and is a treatment based on ancient Chinese Medicine. Over its long history, acupuncture has diversified and nowadays presents a large vatiety of styles and techniques, including Traditional Chinese, Japanese, Korean, Vietnamese, and French acupuncture, as well as specialised forms such as hand, auricular, scalp and ECIWO acupuncture.

Although in acupuncture manual pressure, electrical stimulation, magnets, low-power lasers [107-109], heat, and ultrasound are used , the most frequent and best studied application is the insertion of thin, solid, metal needles, manipulated by hand and/or electrically stimulated.

Although the actual origin of CM remains unclear, it seems that CM has a history of more than 5000 years [3]. There is no single archaeological finding that points to a momentary emergence of acupuncture. Rather evidence exists for a variety of potential antecedent practices like bloodletting, tattoos for religious purposes, and use of bones to extract abscesses [110].

Two very different books are considered the oldest written sources of Chinese Medicin :

A: The Huángdì Nèijīng Sùwèn (黃帝內经素问) The„Yellow Emperor´s Classic on Internal Medicine“ dates back to 206 BC although the Yellow Emperor, Huang Di, the originator of traditional Chinese medicine lived in 2697 BC. This collection of 81 treatises is divided into two parts [111] and can, as far as its importance goes, be compared to the Hippocratic Corpus in Greek medicine [5].

B: The I Ging 易經 / 易经 (Book of Changes), that is considered the oldest book of mankind, dates back to 475–221 BCE. This book, contains mathematical knowledge of binary numbers [4] yang and yin as I/0.

The German philosopher and mathematician Gottfried Wilhelm Leibniz (1646-1716), decoded this binary number system of the I Ging. He also derived the arithmetic rules for calculation with binary numbers (Fig. 3, right) from the I Ging, which makes it possible to describe circular processes.
Leipniz developed from it both the mathematical foundations of information technology and the decisive main ideas for his most important work, the Theodicee (Fig. 3, left).

Basically, these numbers can be composed by yang and yin as I/0 to form bigrammes (numbers I-IV), trigrammes etc. Traditionally, these numbers are represented as a solid line (yang) or broken line (yin). So, in addition to the general and philosophical meanings, yin and yang have a technical application as a numbering system. Circular processes have been described in this way since classical times.

Herrn Gottfried Wilhelms
Freyherrn von Leibnitz
Theodicee,
das ist,
Versuch von der Güte Gottes,
Freyheit des Menschen,
und vom Ursprunge des Bösen,
bey
dieser vierten Ausgabe durchgehends verbessert,
auch mit verschiedenen Zusätzen und Anmerkungen
vermehret von
Johann Christoph Gottscheden,
Statt einer Einleitung ist die Fontenellische Lobschrift
auf den Herrn von Leibnitz neu übersetzt.
Hannover und Leipzig,
In Verlag sel. Nicol. Försters und Sohns Erben.
1744

Einige Beylagen. 823

0	0	1011	11	10110	22
1	1	1100	12	10111	23
10	2	1101	13	11000	24
11	3	1110	14	11001	25
100	4	1111	15	11010	26
101	5	10000	16	11011	27
110	6	10001	17	11100	28
111	7	10010	18	11101	29
1000	8	10011	19	11110	30
1001	9	10100	20	11111	31
1010	10	10101	21		

Dieß ist das Numeriren der Arithmeticae binariae, nun folgen die vier Rechnungsarten:

Fig. 3 The Theodicee, the main work of Leibniz. Above left: Cover of the Theodicee, the main work of Leibniz. Above right: Extract from Leibniz' work showing the character of 0/I. He is quoting the arithmetic rules of binary numbers ("arithmeticae binariae").

The importance of acupuncture as medical therapy emerged around the same time that Confucianism and Taoism gained prominence in China. These philosophies are imprinted in the fundamental principles of acupuncture theory, and their influence is patently evident throughout the ancient texts [110, 112].

The two philosophies, particularly Taoism, emphasized the importance of understanding the laws of nature and for humans to integrate and abide by these laws rather than to resist them. The human body was regarded as a microcosmic equivalent of the macrocosm or the universe. For this reason, concepts used to explain nature, such as yin/yang and the Five Elements (described below), became central to acupuncture theory [112].

1.2.1. Three important concepts in acupuncture

1.2.1.1. The Qi

The Qi is frequently translated as "vital energy" [117]. It is felt to permeate all things, may assume different forms, and travel through energy-conduits, so called meridians, located on the body. It can take the different forms of stagnant, depleted, collapsed, or rebellious.

1.2.1.2. Yin and Yang

Yin and Yang are felt to be complementary opposites and are used to describe all things in nature. Yin is used to represent more material, dense states of matter while yang represents more immaterial, rarefied states of matter [118]. The interplay between the two opposites is dynamic and cyclical.

1.2.1.3. The Five Elements

The Five Elements are wood, water, fire, earth, and metal. These elements are not basic constituents of nature, but represent different basic processes, qualities, or phases of a cycle [118]. Each element can generate or counteract another element. Most vital organs, acupuncture meridians, emotions, and other health-related variables are assigned an element, thus providing a global description of the balancing dynamics seen in each person. (Table 2)

Five Element Theory Chart

Element	Organ	Bowel	Surface Part	Opening	Trait	Mental Part	Taste
Water	Kidneys	Bladder	Bones	Ears	Fear	Will Power	Salty
Wood	Liver	Gall Bladder	Nerves	Eyes	Anger	Mental Activity	Sour
Fire	Heart& Sexual Glands	Small Intestine	Blood vessels	Tongue	Arrogance & Impatience	Intuition, Joy, Peace	Bitter
Earth	Spleen & Pancreas	Stomach	Muscles	Mouth	Worry	Pondering	Sweet
Metal	Lungs	Large Intestine	Skin	Nose & Sinuses	Sadness	Orderliness & Rightness	Spicy

Table 2 Five Element Theory Chart

Within the following 1500 years acupuncture underwent significant development and expansion and was at its climax in the Ming era (1368-1644) when The Great Compendium of Acupuncture and Moxibustion was published in 1601 [113]. Afterwards, it experienced rising and falling popularity due to political and social pressures arising from Western influences.

Acupuncture was disseminated to Korea and Japan in the sixth century, to Southeast Asia around the ninth century through commercial trade routes from China, and to Europe as early as the sixteenth century when Asian texts and translations were brought back by traders and missionaries [114].

Acupuncture became relatively established in some parts of Europe, such as France, around the eighteenth century and persisted due to perpetual colonial influences (e.g. Indochina) [112]. In the United States, traces of acupuncture appeared as early as 18th century and appeared in the early editions of William Osler's Principle and Practice of Medicine [115]. However, acupuncture did not enter the mainstream until 1971, when a New York Times journalist, James Reston, visited China and reported his experiences with acupuncture for postoperative pain relief [116].

In China Acupuncture gained a modern resurgence after Mao ZeDong encouraged its use

among "barefoot doctors" [110] in order to provide basic medical care for the population in China which at that time was a developing country.

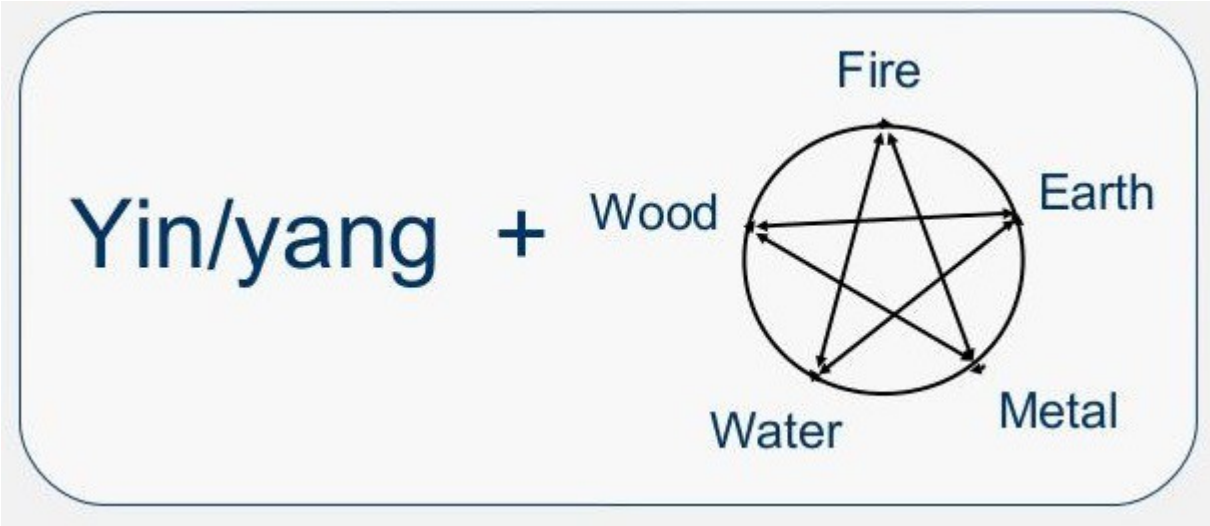


Fig. 4: Pseudo Philosophy of TCM (Greten 2008). The sheng or ko-cycle originates in the 3rd century bC. Feature constellations of clinical signs were arranged according to “elements” and balanced against each other.

In the 1950s to 70s the theory of TCM started to be based on this representation that largely reduced acupuncture diagnostics in order to provide a tool of basic medical care for masses and a rapid distribution of pragmatic concepts.

Therefore, “Traditional Chinese Medicine” (TCM) originally describes the modern practice of CM as a result of widespread reforms that resulted in a certain reduction of the theoretical and diagnostical background. The term “Classical Chinese medicine” (CCM) often refers to medical practices that are based on theories and methods dating from before the fall of the Qing Dynasty (1911) [6]. The apparent irrationality of the shortened versions of TCM exported after the 1950's from China can give rise to misunderstanding which is against a comprehensible theoretical basis for this medical system [3]. On the basis of the pioneering works of the medical-sinologist Prof. Manfred Porkert [120-125], the Heidelberg Model was developed by Prof. Greten [129] as a scientific model to allow rational access to Chinese medicine.

1.2.2. The Heidelberg Model of Traditional Chinese Medicine

An “Integrated Chinese Medicine” or integrated TCM refers to more comprehensive recompilations based on TCM and the current status quo of methodologies. The theoretical basis of such recompilations such as. the “Heidelberg Model of TCM” [2, 4] are mathematical models on vegetative regulation inherent in the classical corpus medicus. In this approach, certain technical terms like yin, yang and the phases can be translated as vegetative functional terms. This can be considered crucial for the integration of TCM in Western health care systems and research. .

Since Prof. Porkert devised a systematic account of Chinese Medicine theories, based on primary Chinese sources, he used a precise terminology in Latin, which better defines the original Chinese concepts at a philological level (e.g. the latin terms calor or algor, meaning “heat/cold”). Accordingly, the Heidelberg Model makes use of this terminology.

Based on the already cited ‟ analysis of the I Ging (“The Book of Changes”), Prof. Greten developed a novel recompilation of the central ideas of Chinese Medicine, thereby explaining it as a logical model of system biology based on a mathematical language [119]. There is evidence that in classical China, even before the Yellow Emperor‟s Classic, these regulatory fluctuations were described by circulatory functions in a simplistic manner resembling a sinus wave. This wave is part of the so-called monad (Leibniz) or Taiji sign. (Fig. 5)

Fig. 5 The Taiji sign

1.2.2.1. The guiding criteria: four different physiological levels

In TCM four main descriptive models have evolved to organize the complex relationships of body regulation. These central ideas are condensed in the theory of the so-called guiding criteria (bagang). In essence these models describe the guiding criteria in the regulation of the human body at four different physiological levels, which together constitute a complex regulatory network model. (Fig. 6)

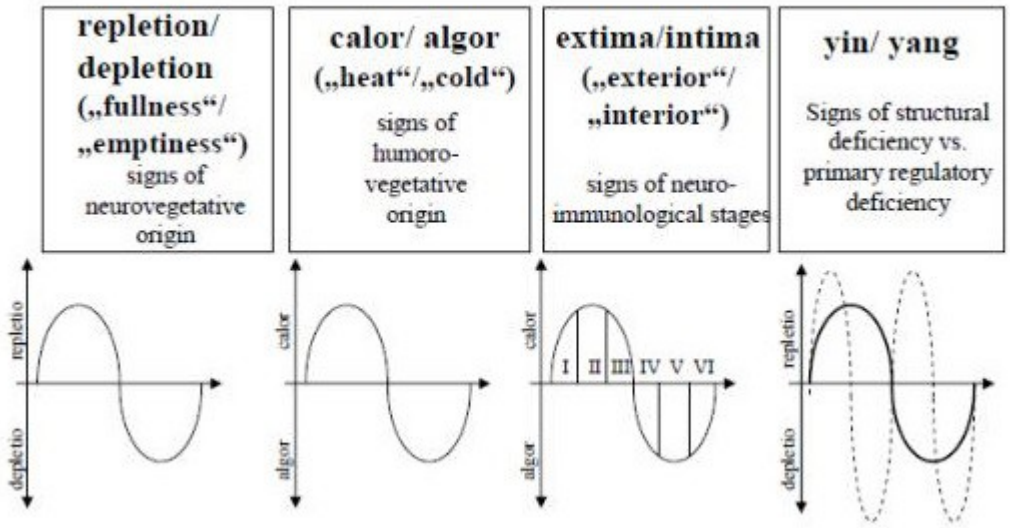


Fig. 6 The Heidelberg Model of TCM establishes a parallelism between TCM concepts of disease and physiological processes at four levels of regulation: neurovegetative, humorovegetative, neuroimmunological, and cellular level.

These four levels of control are: the neurovegetative level, humorovegetative level, the neuroimmunologic level, and the cellular level. (Table 3). The guiding criteria are considered to be an extension of the vegetative regulatory curve on processes such as microcirculation ("heat/cold"), defense mechanisms (theory of six stages of the Shan Han Lun) and the relation of the amount of the cell population and the respective regulatory processes (the yin, "substance") [126].

Chinese Guiding Criterion	Level of Regulation	Physiological Process	Chinese perception
repletio („fullness“)	**1. neuro-vegetative regulation**	Increased activation by the nervous system	„to much capacity to function („qi“) in body and circuits”
Depletion („emptiness“)		decreased activation by the nervous system	„insufficient capacity to function („qi“) in body and circuits”
Calor/heat	**2. humoro-vegetative regulation** („interplay of plasma, endothel and parenchyma“)	increased microcirculation with pro-inflammatory effects and raised sympathetic tone	excess activation of xue/blood (blood and its effects)
Algor/cold		decreased microcirculation with lack of inflammatory effects and sympathetic tone	insufficient activation of xue (blood and its effects)
Extima/outside	**3. neuro-immuno-logical regulation**	early stages of disease	defence mechanisms active on the surface of the body
Intima/inside		late stages of disease	defence mechanisms active in the depth of the body
yang (problem of the degree of unfolding function)	**4. cellular mechanisms**	control of functional tissue defect from outside	problem on the levels named above
yin (problem of the functional tissue)		defect cellular control of the functional tissue	problem resides in the cellular functional tissue, in the degree of hydration or in tissue supply

Table 3 . The Heidelberg Model of TCM establishes a parallelism between TCM concepts of disease and physiological processes at four levels of regulation: neurovegetative, humorovegetative, neuroimmunological, and cellular level.

1.2.2.2. The orbes: physiological patterns

The laws of regulation indicate that most of the regulatory processes are based on periodic fluctuations of the actual value around a target value of regulation. Applying this model of regulation of Chinese Medicine to the vegetative system it results in the categorization of symptoms in organ patterns or orbes (= orbs). “Organs patterns” can be understood as physiological patterns of vegetative origin allowing to translate ancient Chinese physiology in terms of western vegetative physiological knowledge [126].

The technical and regulatory dimension of Yin/Yang and the phases (elements) i.e., Wood, Fire, Earth, Metal, Water, can be seen in an analogous example of the regulation of temperature in a water basin by a thermostat system. Due to the inherent fluctuations, the actual temperature value moves around the set point approximately in a sinus wave. (figure 7).

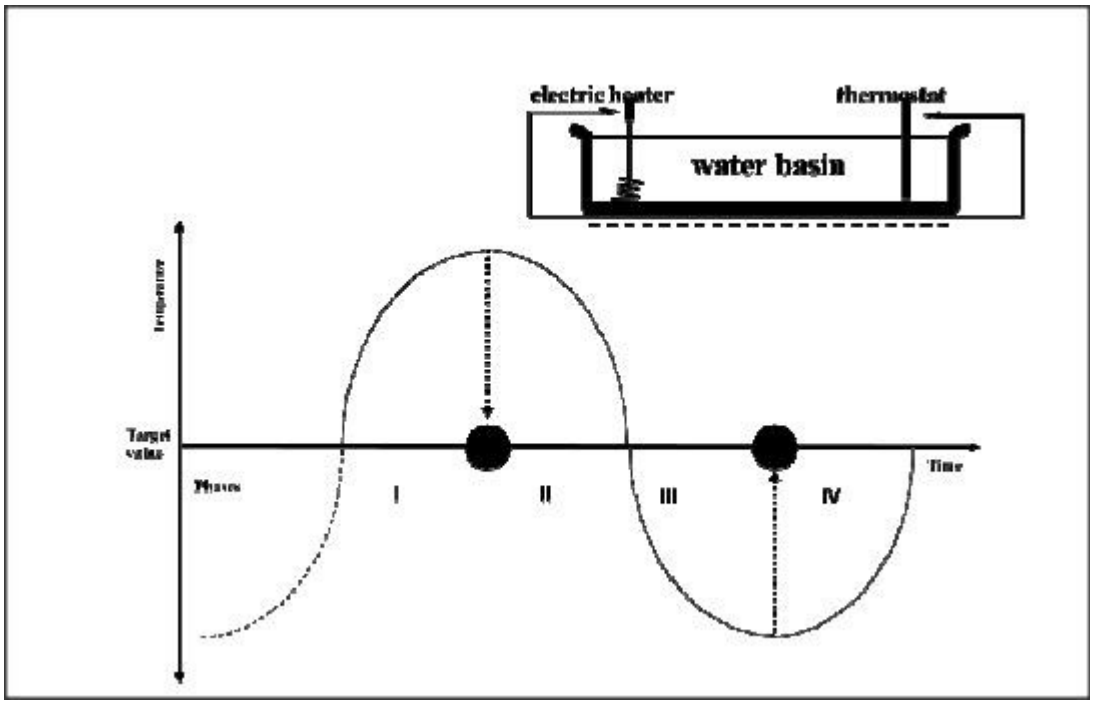


Fig. 7. Regulation as a technical process. The temperature profile of the pool is not constant (straight line), but rather sinusoidal. Temperature is on the y-axis, time on the x-axis, which corresponds to the desired temperature.

1.2.2.3. Sinusoidal-pattern of phases

Almost all biological systems are regulated. in such a sinusoidal course. TCM has developed its own language to describe such changes around the set point, which could be applied to the regulation of the autonomic nervous system in the human body: Yang-states are above the set point; Yin-states are below the set point. The phases designate the sections (quadrants) of this sinusoid curve. A sine curve can also be seen as a circular function. as in the Fou qi character who has the basic mathematical meaning of the description of a circular motion. (Fig. 8).

Yang includes the wood and fire phases; yin includes metal and water phases. This model also illustrates very clearly the concept of Yin-deficiency and the six-stage theory of the “Shang Han Lun” [119].

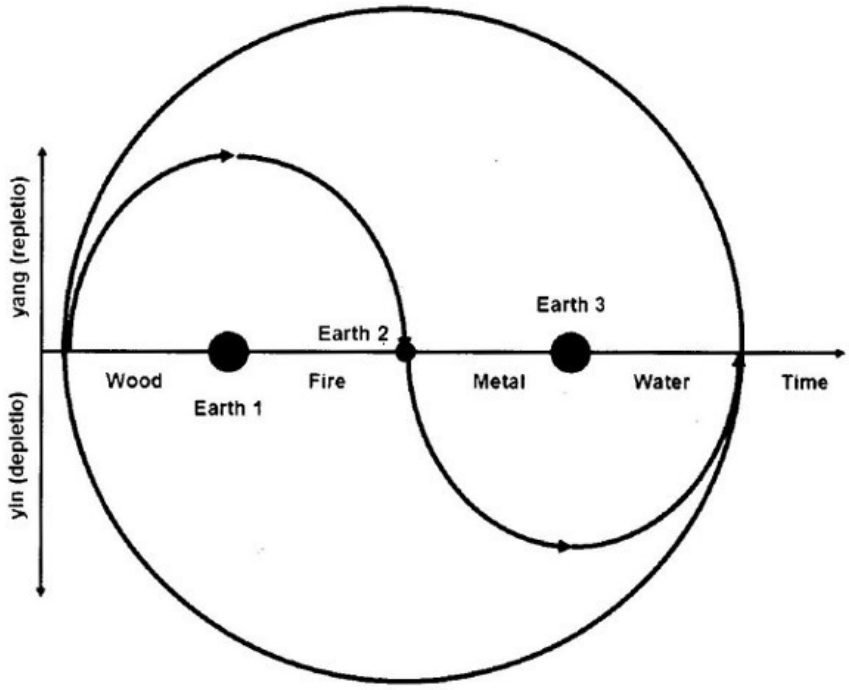


Fig. 8 fou qi emblem: a symbol for the regulatory meaning of yin, yang and the phases

The sinusoid wave is a circular function around a shall-be value in biological systems. Yin and yang are terms of regulation that can be further differentiated in phases (wood, fire metal water) The shall-be-value is associated with the central phase of earth.

1.2.3. Analogies of the phases with neurohormonal mechanisms

The Heidelberg Model hypothesises a relation between this sinusoidal-pattern of phases and the differential activity of the autonomic nervous system and its major molecular effectors (e.g. hormones, neurotransmitters, etc) (Fig. 9).

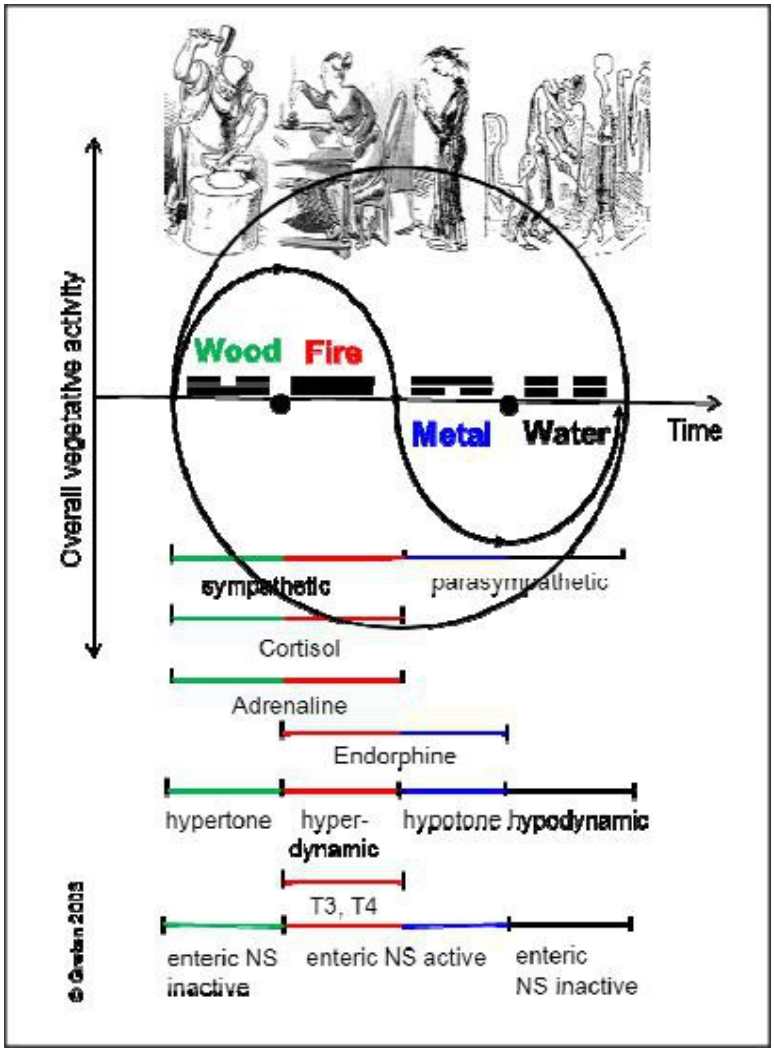


Fig. 9 Vegetative activity

Postulated assignment of phases of Chinese medicine into the autonomic nervous system with respective analogies between the phases and the neurohormonal mechanisms. W – Wood phase. F – Fire phase. M – Metal phase. Scientific proof of efficacy based on this model has been reached by a novel double and even triple blinded assay of evaluation in acupuncture research. [119] have shown that in double or triple

blinded study design, acupuncture based on this reconstruction of classical theory is almost double as effective as current “western” acupuncture . Analogue data has been shown for polyneuropathy [127], in congestive heart failure[128, 129], pain following sternotomy in heart surgery, respiration after heart surgery, pain after tonsillectomy [120], walking distance and peripheral arterial occlusive disease [126]. Nevertheless more studies are needed to support this model.

1.2.4. Diagnosis according to the Heidelberg Model of TCM

Along the lines of this model, the Chinese Medicine functional diagnosis is composed of four steps (Fig. 10):
(A) the constitution; (B) the agent (pathogenic factor); (C) the “orb”, (D) the guiding criteria.

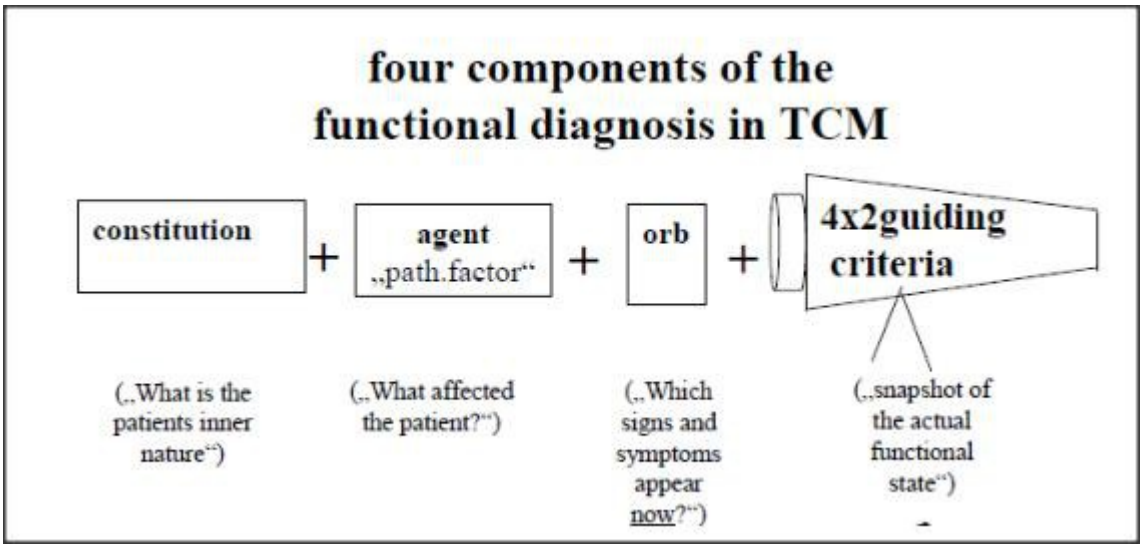


Fig. 10 Schematic representation of the TCM methodology of diagnosis

1.2.4.1. Constitution

Refers to the individual functional properties and the inner nature of the patient based in his/her phenotype. It describes the vegetative reaction type of the patient including a behavioural and emotional typology (the “inner nature” of the patient). Constitution significantly determines expressivity (including pain experience), body tension,conflict processing patterns, the guidance of joints by connective tissue (e.g. in hyper mobile spine), relationship and bondage intensity up to bondage addiction, co-addiction and

tendency to particular forms of compulsion (pulmonary and renal compulsions).

1.2.4.2. Agent

Agent is regarded as a functional power (vector) that changes the individual functional properties (caused by the constitution), produces clinical signs of its own and induces groups of diagnostically relevant signs called “orb” (vegetative patterns). Agents may be divided into:

Exterior agents :wind (ventus), cold (algor), dryness (ariditas), summer heat (aestus), glow (ardor). Exterior agents are vegetative reaction types of the defence type against cold, draught, humidity etc.

Interior agents :(Ira (“anger”); Voluptas (“lust”); Maeror (“grief”), Timor (“anxiety”); Pavor (“shock”); Solicitude (“worriedness”); Cogitation (“thinking”). Interior agents are emotions

Neutral agents: overwork, physical effects, poisoning.

The agent as pathogenic factor is the „trigger of disease“ that causes the symptomatic state of a patient. The agent primarily determines the modalities of pain, such as worse on cold, worse on change of weather, worse in draught etc. Each agent is defined by key symptoms (Table1) and is accompanied by typical forms of general condition and typical tongue and pulse patterns. (Table 4)

Agent/ Pathogenic Factor	Ventus/Wind	Algor/Cold	Humor/Humidity
Symptoms	„as if you had been exposed to a draught of air"	„as if you had been exposed to environmental cold"	„as if you had been exposed to environmental humidity"
Reflex pattern	Reaction of the draught defence type	Reaction of the cold defence type	Reaction of the humidity defence type
Postulated Mechanisms	Substance P- mast cell reflex old reflexes of motor control as known from fish and other species	Local microcirculation disorder	Pre-oedema or oedema
Reaction pattern in the direction of	Yang (repletio, Wood)	Yin (depletio, Metal und Water)	Yin
Skin	Warm and sweaty	Cold and dry	Bloated, doughy, sticky
Tongue	„raspberry dots"	Hyaline coating (bloodless gel-like)	Sticky coating, tooth impressions
Character of pain	Sudden onset, shooting	Gradual onset, tearing	dull
Muscles	Spasm, myogelosis	Muscles not stretchable, rigid	Swollen, feeling of heaviness
General condition	Driven	Exhausted	Dyspnoea, feeling of heaviness

Table 4 The agents

1.2.4.3. The Orbes

The orb is the clinical manifestation of a phase, named after a region of the body. It consists of a group of diagnostically relevant signs indicating the functional state of a body island that correlates with the functional properties of a phase. (Dr. Greten 2007)

It is the current disturbance pattern which also includes the current main symptom. Symptoms are considered to be part of a group of pre-defined diagnostic signs. These signs, “organ patterns”, “functional circles” or (latin) orbes are an expression of body regulation named after organ regions (body islands) which can become symptomatic within the overall pattern.The orb (e.g. the hepatic orb) manifests a vegetative functional tendency which is called phase (e.g. wood).

1.2.4.4. Guiding-criteria (GC)

The guiding-criteria (ba gua) are regulatory models of physiology, that allow the interpretation of the actual symptoms on the background of overall body regulation.

First: GC repletio/depletio ("excess/emptiness")
It evaluates clinical signs that in Chinese Medicine are believed to originate from qi and orbs and phases. In western terms, these signs are of primary neurovegetative origin. In general, signs of repletio indicate too much qi in the organism as the origin of symptoms. Repletion is analogous to relative over-excitation of neurovegetative activating mechanisms. Sings of depletion indicate lack of qi. Depletion is a lack of respective activation or excess de-activation.

Second: GC calor/algor" („heat/cold").
It evaluates signs which in Chinese medicine are believed to originate from the effects of xue ("blood") which is the second power ("energy") of Chinese medicine. From a western medical view, it refers to clinical signs predominantly originated from the humorovegetative system. The GC calor/algor reflects

(1) the effect of microcirculation within the disease on a systemic and regional level (local interdependent mechanisms of the plasma, blood cells, endothelium, and functional tissue);
(2) the activation of body fluids, evoking vegetative and systemic responses in the context of fluid distribution, fluid supply and circulation (e.g. changes in thirst, urine output, heart rate). Signs of over-activation of xue are called "calor"; signs of a lack of functional microcirculation are called "algor".

Third: GC extima/intima ("exterior/interior").
It evaluates signs that in Chinese medicine are believed to originate from the effects of a pathogenic factor (agent) invading the body from the exterior. The most common pathophysiological model behind it is the model of the six stages (Shang Han Lun), the process of the agent "algor damaging the body" or "algor laedens theory" (ALT), according to Prof. Porkert. From the western perspective, it refers to clinical signs induced by neuroimmunological mechanisms.
In case of algor affecting the system, a regional lack of microcirculation may be caused by

defense reflexes to cold, by viruses (adhesion molecules, complement system, coagulation); the counter-reaction consists of a general increase in microcirculation, inflammation, fever and sepsis. This counter-reaction is called “reactive calor” and is a regulated process in itself.

Fourth: GC:s yin/yang.

It evaluates signs which, according to TCM, distinguish between primary deregulation (yang) and secondary deregulation due to structural deficiency (yin). (Table 5) If a functional tissue is deficient, it will be excessively up-regulated to achieve appropriate function. As this augmentation of tissue function cannot be kept up, functional deficiency follows. From the western perspective a deficient cell population can be vegetatively overstimulated causing vegetative clinical signs named under repletion.

Thereafter, a phase of almost functional break-down may arise with signs similar to depletion. As such, in diseases described by yin, symptoms are due to deficiency of the functional tissue (“body substance”, yin). Other types of yin deficiency may be due to lack of Xue (lack of microcirculation within the tissue), lack of body fluids (lack of milieu-factors), lack of jing (functional deficits like in impaired functions of the cell nucleus, or in genetic deficits) In yang-diseases symptoms are due primarily to deregulation described by the first three guiding-criteria.

Chinese type of yin deficiency	Comment from western medical view
yin deficiency “sui generis”	lack of “functional tissue”
lack of xue	“lack of microcirculation within the tissue”
lack of body fluids jin ye	“lack of milieu- factors” such as in dehydration
lack auf jing	“functional deficits” like in impaired functions of the cell nucleus (i.e. radiation, chemotherapy) or in genetic deficits

Table 5. Guiding criteria and their significance in determining the overall regulatory status (Greten 2008). Levels of regulation (in western language) and their analogues in Chinese medical theory in a first approach

1.2.4.5. The Algor Laedens Theory ("harmful cold disease") = ALT

According to Prof. Porkert, the ALT is the most common pathophysiological model that explains the process of "cold-invading" diseases in TCM, which have a parallel on clinical signs induced by neuroimmunological mechanisms on a Western perspective. The ALT assumes that in case of "algor" affecting the body system, a regional lack of microcirculation may be caused by defence reflexes to cold, by viruses (adhesion molecules, complement system, coagulation). The counter-reaction ("reactive calor") that takes place consists in a general increase of microcirculation, inflammation, fever and sepsis. The agent invades from the extima to the intima, thereby overcoming the defence levels and revolving the flow of qi and xue. The stages I to III of ALT are interpreted as extimal (yang) stages. In this logic stages IV to VI are intimal (yin).

The ALT combines the language of the orbs (neurovegetatively originated signs) with the language of the system of calor/algor, a part of neuroimmunology, and reflects the functional activity of the defence mechanisms expressed by calor (yang) and algor (yin).

The six stages of the ALT are syndromes composed of specific signs of two orbs, each. According to the model, the six stages form a complete circle of stages of an infectious disease. During the course of such cyclic process, an individual usually overcomes the infection and remains healthy thereafter. However, under certain circumstances, some signs of the six stages may remain and become chronic, such as in cases of fibromyalgia, rheumatic disorders, osteoarthritis, or chronic inflammation.

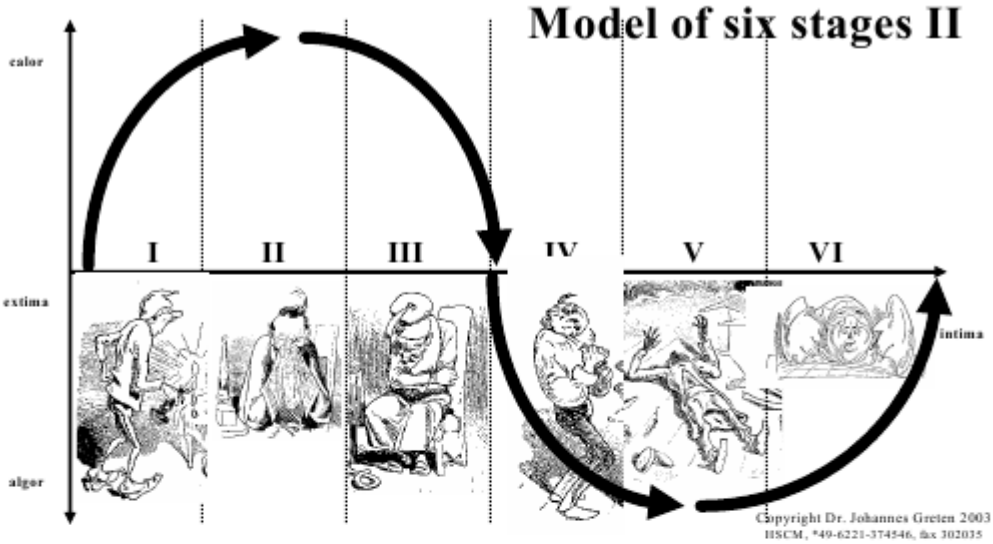
1.2.4.5.1. The three Yang/ Extimal Stages

Yang stands for extima, for activity in general and within the meaning of the phases it stands for reactove calor.
This is why among the first three stages, Stage II with the highest calor in the clinic is characterised very often by too much calor, this reactive calor being responsible for most of the symptoms. This over-riding, over- extensive calor is called yangming in Chinese, whose Latin transcription is splendor Yang (Stage II).In comparison to this splendor yang stage, the two other extimal stages can be divided into the yang that rises, Taiyang (Stage I) or in Latin the Yang major; and the lesser yang, Shaoyang, Yang minor (Stage III).

1.2.4.5.2. The three Yin/ Intimal Stages

Within the yin, the intimal phases, the reactive calor is deficient resulting in internal algor; which could be defined as a yin state or a state of deficient functions that are under the target value of the production of warmth and heat.
In this context, the target value stands for a balanced temperature behaviour of the body.
Besides the hypofunctional state, the term yin also refers to the body substance, yin. The most pronounced lack of function seen in Stage V, where the substance is used up, is called Jue yin in Chinese and in Latin Yin flectens meaning that the yin “goes away”, vanishes, but also represents a turning point of the disease when it becomes life-threatening, dangerous and critical. The other two stages are, again, named in a comparative manner in relation to the acute Stage V. Thus, Stage IV, where there is more substance blocked, more yin is called the bigger yin, Taiyin, yin major; and the stage where there is less substance left, the yin is smaller is named the smaller yin, Shaoyin, Yin minor – Stage VI.
Another major aspect is, that yin major has a downward direction, which means that the hypofunctional state of internal algor is becoming more pronounced, “more yin” or yin major. In stage VI, yin minor the hypofunctional yin state has an upward direction comparable to the phase of water (regeneration) in the model of phases, having the capacity to regenerate to normal.

« ALT » algor laedens theory	stage 1 = yang major taiyang	stage 2 = splendor yang yangming	stage 3 = yang minor shaoyang	stage 4 = yin major shaoyin	stage 5 = yin flectens jueyin	stage e 6 = yin minor taiyin



Symptoms of phases „catchword“	„Sciatic and ear pain“	„Acute sinusitis“	„Hot-cold-nausea-phase“	„Mucus and bronchitis“	„Flat-down-phase“ („pneumonia“)	convalescence
Involved conduits and orbs	V - IT	IC - S	F - TK	P - L	H - PC	R - C
Linked conduits and orbs	R - C (2nd circuit)	P - L (1st circuit)	H - PC (3rd circuit)	IC - S (1st circuit)	F - TK (3rd circuit)	V - IT (2nd circuit)
Exemplary decoction	Dec. Ephedrae, Dec. Ram. Cassiae	Dec. Ancillae Yue	Dec. Bupleuri	see text	see text	see text
Variation I: energetic factors determining the course	Lack of xue and defensive-qi: more prone to phase 1	Additional ventus: even acuter calor	Weakness of orthopathy (qi): faster transition into phase 4	Lack of qi worsens the course, as P und L are qi-dependent	Mare xue: part of hepatic yin, therefore worse, if xue deficient	Yin (body substance) is decisive
Variation II: „outside-inside hopping“ or „inside-outside-hopping“	If yin is extremely weak: direct transition into stage 6 possible	If lack of qi and depletion of the centre: direct transition into stage 4	If lack of qi and xue: direct transition into stage 5	“sinu-bronchitic syndrome” (transition from stage 4 to stage 2)	stage 5 may go over into stage 3, i.e. as a form of recovery in pneumonia in the elderls	In stage of recovery: i.e.still aching limbs of algor kind (1. stage)
Variation III: add. ventus	All phases tend to show more signs of yang, repletion and especially more CALOR!!					

Fig. 11 ALT related orbs and cross-linked orbs. Energetic factors determine the course. Variations in the course: outside-inside and inside- outside hopping. Gretten 2010.

1.2.4.6. Four kinds of mechanisms may cause disease according to TCM on a dogmatic level:

(1):excess of an agent;
(2) transitional problems from one “evolutive phase” to the next;
(3) imbalance of antagonist phases;
(4) yin deficiency.
I
In summary, Chinese Medicine developed as a doctrine based on clinical signs which allow the definition of the regulatory status of the individual. Chinese Medicine can be considered a vegetative medicine, largely based on reflexology and a rational theory of vegetative (autonomic) nervous system activation patterns.

1.2.4.7. Pain according to Heidelberg model of Traditional Chinese Medicine

The following text is an excerpt from an unrevised course syllabus by Prof. Greten (2007)

The origin of pain

In Chinese Medicine pain is believed to be the consequence of a lack of qi flow. If this qi flow is blocked for a longer time, even xue will not flow, resulting in xue stagnation and finally xue stasis. The symptoms of disturbed qi flow are pain and functional disorders.

It is known to the west that inhaling provokes a little rise in sympathetic tonus and exhaling produces a lower sympathetic drive and higher vagal tonus. Like this, the motion of breathing in fact stimulates and deactivates all tissues of the body. As qi flow, according to our model, shares many analogies with vegetative activation patterns, this explains the role of the pulmonary orb in

- distributing qi and
- controlling the movement of qi.

In fact, it is said that the lungs are "the pump of qi" in the body. This applies to the whole body and as the qi flow within ihe body is mirrored on the surface, proper breathing is believed to be the basis for qi flow in the conduits, too. This explains how the pulmonary

orb controls the extima on the whole.

Actually it is believed that the puimonary orb, which we roughly translate as the many effects of the breathing movement, also rules the defensive qi. This defensive qi is not located in the conduits but in the surrounding tissue in the whole body. It is especially important in the extima where for natural reasons the defence must be strong, as it is the protective wall of the body.

The breathing movement is stimulating the extima. The pulmonary orb controls and distributes the defensive qi. If this qi is low, external agents can invade more easily. Many patients with chronic pain syndromes or recurrent infections like children have an improper breathing. The spatial patterns of stimulation and de-activation of tissues that come by the breathing movement may help us to understand how pain is generated.

Chinese Medicine states that spatial distribution pattems of activation (qi flow) are blocked when pain comes. This can be explained by a lack of spatial distribution of the effect of breathing, the spatial wave of vegetative activation. In this sense, the pulmonary orb acts as-a wiper of the human windscreen. Breathing has a cleaning effect on the whole conduit system according to the core statements of Chinese Medicine.

When the transition of this vegetati ve is blocked for whatever reason, this may lead to non-transition of the wave from one part to the other of the body. So the transition trom one tissue to the next of this vegetative action does not take place. Accordingly, the orver-activating effect is seen in the tissue which is located before the site of transition.

In Western terms, neuro-impulses, which should evenly distribute over the tissues, then concentrate on one tissue, a site of the body that finally is felt as painful. The threshold for the feeling between over-activation and pain varies individually. But if there is over-stimulated tissue, this is, according to our experience, correlating with repletive pain. This kind of pain becomes worse under pressure. and we, use dispulsive needling to cure it. Dispulsive needling therefore could be explained as lowering the sympathetic activation pattern within a tissue that depends on a certain point.

On the other hand, depletive pain may be due to a lack of stimulation. This kind of pain is also believed to be produced by blocks of qi. It may be explained, in a Western sense, by

the fact that after the site of blocked transition of the spatial wave of neuro-activation there is a lack of sympathetic action and a relative over-representation of vagal and de-activating stimuli.

Letting a needle reside in a certain point is called suppletion. This effect may be explained by a stronger perception of the dependent area by the central nervous system. Like this, the sensation of stimulation is directed to the area. This is why the subconscious “focuses” on this area resulting in a regulation of the feedback mechanism of vegetative impulses'

This is consistent with the finding that oniy thinking of an acupoints can have an effect. Acupuncture as a reflex ttherapy can therefore be regarded as a functional vegetative therapy. Western medical language calls this vegetative spatial distribution of impulses whereas the Chinese explanation is qi flow. Therefore we believe that most of the effects that are thought to be caused by qi are simply neurovegetative in origin. This supports the Heidelberg Model which argues that the core termini of Chinese Medicine - the phases and yin and yang - and the patterns which we call orbs are vegetatively explainable by the cybernetics of the phases that we teach.

The spatial distribution of neurovegetative impulses therefore causes sensations of pain and the question arises how this is generated. Chinese Medicine says that external agents contribute significantly to this block of qi. The present understanding of the external agents is that these agents in fact do not invade the body like "wind" enters the body, but that vegetative reflex pattern are elicited that are similar to the influence of draught on the body, of cold and therefore represent vegetative reflex patterns, too.

Ventus, e.g., may be explained by the effect of substance P on mast cells and by eliciting motion patterns which may be derived from evolutionary swimming movements.

"Cold" (han, algor) e.g. can be explained by shutting the capillary flow in certain areas. We could therefore postulate that these disturbing patterns may be so strong locally that the normal spatial distribution of neuronal stimuli is not possible and overlaid by he physiological reaction and reflex pattern which is called an agent.

There are stages of pain origin in Chinese Medicine that we have referred to previously: a

block of qi flow, xue stagnation and xue stasis. Block of qi flow, as explained, naturally shows a combination of pain sensation and dysfunctional tissue behaviour.

Of course, lack of stimulation or over-stimulation of a certain tissue will also affect the capillary flow. The capillary flow, as we have seen above. is largely due to the breathing movement which is called pulmonary orb, he pump of qi and xue within the body in Chinese Medicine. Activated tissue will need more oxygen and more blood flow in the capillaries, de-activated tissue will show less blood flow. This is why repletion corresponds to calor and sometimes even to ardor and depletion corresponds to cold patterns.
Stagnation of xue is comparable to a slight venous congestion of the microcirculation and the clinical signs according to Chinese Medicine are livid tissues and tissues that show dark blood flow out of the point into which a needle was insertedyou have inserted a needle. The flow of blackish blood is therefore a sign of xue stagnation in the dependent tissues. Stagnation of xue, according to Chinese Medicine, can accumulate and ascend to real acute stasis. The symptom of this is acute pain of stabbing nature. Outflow of'red blood from punctured sites is an important sign of this acute stasis. We can therefore postulate that capillary flow is intended to be augmented by the body which we call reactive calor. Most probably the mechanism by which stagnation of xue turns into stasis of xue is that the stagnation of blood flow, of xue, is enhanced. So we have something like a microcapillary microthrombosis. Therefore, the reaction of the surrounding tissue is to dissolve this microthrombosis, this intravascular coagulation.

Some arguments may be put up to underline this.

l. Disseminated intravascular coagulation (DIC) is one of the key features in sepsis and shock. These are also believed to be reactive calor which finally leads to collapsing yang. In Western medicine DIC goes along with high mortality which is an analogue process.

2. In Chinese Medicine micro-bloodletting in acupoints is a common technique. It is believed that the most pain improves when you hit the acupoints that lets out blackish blood (venous congestion). The preceding acupoints on the conduit normally show reddish blood. When you hit the point of stagnation and the blackish blood comes out, the outflow of blood from the other points is suddenly enhanced and all colour of the outcoming blood is then coming to normal and is equal in both the formerly blackish and

reddish points. These congestions therefore may be stagnation of xue and may lead to acute stasis by blocking surrounding capillary flow, whether this is directly caused by coagulation or just be blowing up capillaries by congestion so surrounding capillaries are pressed. This remains a field of research.

1.2.4.8. Bi-Syndrome, the TCM diagnosis of chronic pain in the trapeziometacarpal joint

A: Bi-Syndrome = Painful Obstruction Syndrome is the TCM diagnosis for :musculoskeletal disorders causing chronic pain in the the TCM joint (with no correlated radiographic or other verifiable or mesurable diagnostic findings

B: **Bi-Syndrome of bone** is the TCM diagnosis for :
rhizarthrosis or osteoarthrosis of the TCM joint

ad A: **Musculoskeletal Disorders :**

According to traditional Chinese medicine Bi-Syndrome refers to stiffness and blockage of circulation of Qi and blood in the energy leading conduits.
Bi-syndrome involves pain in muscles, tendons, bones and joints as well as difficult movement or deformation of these structures. Bi-syndrome involving the musculoskeletal system is a result of invasion from wind, cold, damp and heat.
Musculoskeletal Bi-Syndrome can be divided into excess patterns associated with wind= ventus, cold = algor, damp= humor and heat= calor

Wind Bi = ventus-Bi

Wind Bi-Syndrome is also called wandering Bi and the patient shows signs of migrating pain. There is invasion of wind-cold- damp, but primarily wind from the exterior. The wind obstructs Qi and blood flow in the muscles, bones and conduits which cause pain.There is a rapid onset of clinical signs of pain in the joints. The pain gets worse when the patient is exposed to wind. The tongue is pale with a thin coating and the pulse is superficial. The treatment principle is to eliminate the wind and invigorate the channels, eliminate cold and disperse damp.

Cold Bi = algor-Bi

Cold Bi-Syndrome is also called painful Bi and the patient shows signs of severe pain.

The primary pathogen is cold and in addition, there is a combination of wind and damp. The coldness obstructs Qi and Blood flow. The joints are painful and there is restriction in their movements. The pain gets worse when the patient is exposed to cold and there is pain relief with heat exposure. The tongue is purple with a slight pale coating and the pulse is wiry and slow. The treatment principle is to eliminate the cold and warm the channels and also clear the wind-damp.

Damp Bi = humor-Bi

Damp Bi-Syndrome is also called fixed Bi and the patient shows signs of marked joint stiffness. The primary pathogen is damp and in addition there is a combination of wind and cold. The damp obstructs the flow of *Qi* and blood. There is more stiffness than pain. The pain gets worse when the patient is exposed to cold and damp conditions and there is pain relief with heat and dryness. The tongue is pale with a greasy coating and the pulse is soft and slow. The treatment principle is to eliminate the Damp and the Wind-Cold.

Heat Bi = calor-Bi

Heat Bi-Syndrome is also called febrile Bi and the patient shows signs of acute onset of local inflammation. The primary pathogen is heat. The wind-cold-damp causes stagnation which turns into heat. The patient has acute inflammation of the muscles or joints and this shows clinically as pain, redness, swelling and heat. The patient may have a fever. The tongue is red with a yellow coating and the pulse is strong and fast. The treatment principle is to clear the heat and eliminate the wind-damp.

Bi yndrome of Bone is a deficiency pattern which includes kidney Qi, Yin and Yang. Bony *Bi* is the most advanced condition and the affected joints have chronic osteoarthritis.

ad B: **Rhizarthrosis** or Osteoarthritis of the TCM joint

The term ‘osteoarthritis’ did not exist in ancient Chinese medical texts, although there were descriptions of diseases that were very similar in terms of clinical characteristics. In

general, OA is usually categorised as ‘Bi-Syndrome’ (painful obstruction syndrome), and more specifically, ‘Bi-Syndrome of bone’.

In modern texts, the term ‘Bi-Syndrome’ describes conditions of pain, soreness or numbness of muscles, tendons and joints as a result of invasion of external pathogenic wind, cold and/or dampness (290, 292). However, the term ‘bi’ is an ancient concept with broad meaning.

In the Huang Di Nei Jing Su Wen (Yellow Emperor’s Inner Classic Plain Questions), one of the key ancient texts of Chinese medicine that is likely to have been compiled during the Han Dynasty, the word ‘bi’ translates as ‘blockage’ (293). Unschuld (2003) explains how within the Su Wen there is evidence of several changes in conceptualisation of the concept of ‘bi’, from a more basic reference to mechanical blockage of the urethra, to its conceptualisation as a disease caused by excessive wind, cold and/or dampness.

In modern CM, ‘bi’ is now used to describe a disease, a set of signs and symptoms, or a term in pathology (293). With respect to Bi as a disease name, this is further specified in terms of the predominant pathogenic factor/qi involved, for example ‘wind block’, or the location of pathology, for example ‘bone block’ or ‘liver block’.

Since pathological changes associated with Bi-Syndrome usually occur in joints and muscles, pain associated with OA typically occurs with joint usage and/or stiffness (294, 295). Other symptoms and signs of Bi-Syndrome include joint disability and/or oedema and numbness (296). In mild cases, there may be pain in the limbs and joints that becomes more pronounced with changes in the weather and, in severe cases, more pronounced soreness and pain, deformities and decreased range of movement (297). However, some patients with radiologic evidence of OA have no symptoms (298).

Lack of pain in some OA sufferers is not inconsistent with descriptions of ‘bi’ in the Su Wen of blocks affecting the bones, sinews, vessels, flesh and skin that do not cause pain (293).

In the two official clinical guidelines from the People's Republic of China, OA and degenerative arthrosis are both classified as ‘Bi-Syndrome of bone’ (299, 300). Aetiology, pathogenesis and treatment of OA. OA has generally been considered to be a type of Bi-Syndrome caused by depletion of the kidney and liver yang, which invites invasion of exogenous pathogenic factors. Such invasion obstructs the conduits, leading to impaired qi and blood circulation and, consequently, pain. In the majority of cases, the external causes of Bi-Syndrome are a combination of three pathogens: wind =ventus, cold=algor and dampness=humor (296).

Impairment of the transformation of body fluids over long periods (due to spleen depletion) leads to stagnation of non-substantial phlegm =pituita. Blood (xue) and phlegm = pituita stagnation become secondary pathogenic factors that accumulate in the joints and further exacerbate the problem (301), with phlegm =pituita condensing to form bone growths (290).

The kidney has traditionally been considered the primary organ involved in the development of Bi-Syndrome, with the liver secondary (302). There are logical reasons for this within CM theory. The kidney is said to dominate bones. The kidney essence (jing) (a vital substance responsible for the formation of bone, growth and development) declines with age, which causes the qi of the organs to become depleted, the bones to become frail, tendons to stiffen and consequently movement to become impaired (292). Osteophytes - outgrowths of bone - are often associated with OA.
The liver is said to store blood and control the sinews (tendons, cartilages and ligaments) through its nourishing and moistening functions. kidney yin is the foundation of liver yin and blood.
The spleen is also involved by virtue of its actions of controlling the muscles and limbs, and transforming and transporting fluids and qi. Spleen depletion can lead to deficiency of qi and blood (since the spleen produces qi), further reinforcing deficiency of kidney jing and liver blood. In addition, the spleen is easily affected by external dampness (292).

1.2.4.8.1. TCM treatment concept for osteoarthrosis

The treatment strategy for OA logically follows the diagnosis and understanding of its pathogenesis. General treatment principles give consideration to the ‘ben’ or root cause of a condition and the ‘biao’ or branch (which relates more to the symptoms and signs). Bi-Syndrome is considered to be a condition where the root is deficient (deficient kidney jing and liver blood), allowing invasion of pathogenic factors and contributing to the pathogenic development of blood and phlegm stagnation. The branch, on the other hand, is often excessive (referring to qi/blood/phlegm stagnation and invasion of external pathogenic factors that cause painful obstruction)
.
As a consequence of this understanding of the pathogenesis of the condition, the treatment strategy of CM has traditionally been to tonify the kidney and liver, nourish qi and blood, expel wind-cold, remove dampness, promote blood circulation and remove

obstruction from the conduits and collaterals. The majority of Chines Herbal Medicine formulas used to treat OA follow this basic pattern identification, and emphasise tonifying the kidney and liver, promoting blood circulation, expelling wind and resolving dampness (303).

Acupuncture has been widely used for treatment of OA of the knee and chronic knee pain (304; 305), and, at least in China, commonly in conjunction with other techniques including electronic stimulation (electro-acupuncture) (306; 307; 308; 309), moxibustion, electrical heat lamps and other special electromagnetic therapeutic apparatus (310; 311; 312), acupoint injection, cupping, physical exercise and herbal medicine (oral, external and/or ionotherapy methods) (313; 314; 307; 308; 309). The technique of 'warm needling' is the most popular treatment modality for OA (315; 316; 317; 318), in keeping with the idea that OA is due to kidney deficiency and invasion of cold and damp (319). Laser therapy is also used for OA treatment in China (320).

Arguments about the classification of OA and emerging theoriesThe main reason for classifying OA as Bi-Syndrome centres on the key symptom of pain. It is not difficult to understand the reasoning behind the primacy of the kidney in the pathogenesis of OA, given the previously outlined theoretical rationale.

However, some researchers have argued that OA should be categorised as a disease of the sinews rather than 'Bi-Syndrome of bone' (301).

The arguments for this include the fact that pathogenic changes of OA occur in articular cartilage and the tissue around joints - which are classified as 'sinews' in TCM and considered to be an extension of the liver.

Inability to bend or straighten a joint properly, or overcompensation in order to do so is a sign of tendon degeneration (292).

Consideration of the function of liver blood suggests a potential pathomechanism: if liver blood is deficient the sinews will lack moistening and nourishment, which may cause contraction, spasm, impaired flexion, numbness of the limbs, tingling and muscle cramps. In addition, if there is stasis of liver blood, the sinews will lack suppleness and the person may experience stiffness, rigidity and pain of the joints (291).A relatively recent emergent theory is that OA should be considered a combination of wei syndrome and Bi-Syndrome, with wei syndrome considered the fundamental disorder and Bi-Syndrome secondary. Thus greater emphasis is placed on the role of the liver in the pathogenesis of OA, rather than the kidney. A key proponent of this theory is Professor Shi Yinyu of Shanghai

Shuguang Hospital.

Wei syndrome is defined as progressive weakening or degeneration of the limbs caused by a deficiency of qi, blood, body fluids and/or jing. It manifests as flaccidity of the sinews or muscles and, in severe cases, loss of voluntary movement of the limbs (322). The following quote from Chapter 44 of the Su Wen clearly links the notion of blockage (described in other parts of the Su Wen in relation to Bi-Syndrome) and muscle flaccidity, a key symptom of wei syndrome:

Signs and symptoms of OA in the initial stage are indicative of 'painful obstruction' (Bi-Syndrome), although the clinical manifestation of advanced OA is atrophy of the muscles of the limbs (from lack of use) - a major feature of wei syndrome - along with muscle weakness.

Other symptoms such as numbness may be shared by both Bi-Syndrome and wei syndrome.

According to TCM theory, by fifty-six years the liver energy weakens causing the tendons to stiffen (292).

Chapter one of the Su Wen states that the kidney qi begins to decline over the age of 40 years (292).

Indeed, the kidney jing and liver blood are understood to have a common source. Therefore the decline in function of the liver and kidney with increasing age, as described in TCM theory, is in keeping with the epidemiology of OA: that approximately 40 per cent of adults over 70 years old are affected by OA of knee, 80 per cent of whom have limitations of movement and 25 per cent of whom cannot perform the major daily activities of living (323).

For these reasons, it has been argued by some that OA should be considered a combination of Bi-Syndrome and wei syndrome (324; 322). This has important consequences in terms of treatment, The treatment principles that follow this reasoning emphasise soothing and nourishing the liver (in particular the liver blood), soothing the sinews and eliminating exogenous pathogenic factors (321). Other authors such as Guo et al. (2002) support the notion that in a chronic disease such as OA, comprehensive treatment strategies are required, and suggest that treatment strategies should encompass tonifying the kidney, soothing the liver, invigorating the spleen and removing blood and phlegm stasis.

1.2.4.8.2. The scientific evidence base of Chinese medicine in OA treatment

In comparison with rheumatoid arthritis, OA has historically not been a priority area for research (325). Studies have found that Chinese Acupuncture is cost-effective and can reduce the burden of OA (326), which was estimated as costing Australia AUD$ 1090 million in 2001 (327).
To understand the scientific evidence base for the treatment of OA with TCM a literature search of clinical studies was made that investigated the efficacy of acupuncture and Chinese Herbal Medicine in treating OA of the knee, a common location for OA.
Literature search revealed 33 clinical trials that have investigated the efficacy of acupuncture in the treatment of OA of the knee (328). Twenty-seven of the studies were conducted in China, all of which found that acupuncture was effective.

One meta-analysis concluded that the clinical improvements due to acupuncture may be due to placebo or expectation effects (329). Another systematic review found acupuncture superior to sham (placebo) acupuncture for treating chronic knee pain in both the short and longer term (295). Systematic reviews of acupuncture studies in OA indicate that there were no associated adverse events (329; 295) and that acupuncture is a relatively cost-effective therapy for OA patients (330).

1.2.4.8.3. Conclusion

How OA is understood and treated in CM is vastly different to Western medicine, which is unsurprising given the very different paradigms of these two systems of medicine. OA is usually categorised as Bi-Syndrome,

1.2.5. Generalities of acupuncture research

1.2.5.1. General proposed mechanisms of action of acupuncture

Multiple physiologic models have been proposed to explain the effects of acupuncture. Various models have implicated cytokines, hormones (e.g., cortisol and oxitocin), biomechanical effects, electromagnetic effects, the immune system, and the autonomic and somatic nervous systems. For many proposed models, the data have been either too inconsistent or inadequate to draw significant conclusions.

1.2.5.1.1. Endorphins

The most thoroughly studied application of acupuncture is for pain relief. Studies performed in the 1970s and 1980s have contributed tremendously to our present understanding of acupuncture's analgesic effects [131-152]. According to this theory, acupuncture stimulation is associated with neurotransmitter effects such as endorphin release at both the spinal and supraspinal levels [153, 154]. In support of this theory, there is evidence that opioid antagonists block the analgesic effects of acupuncture [155]. In contrast to this theory, however, the endorphin effects appear to be short-term, only lasting 10 to 20 minutes and possibly up to several days [156], while many acupuncture clinical trials have documented longer effects [156-158]. Additionally, endorphin release can be induced by strongly stimulating any free nerve ending or muscle afferents. The specificity of acupuncture point location and the rationale for needling certain points in various conditions remain unexplained. For these and other reasons, researchers have acknowledged the limitations of the endorphin-related mechanism [159]

1.2.5.1.2. Functional MRI

Functional MRI (magnetic resonance imaging) studies have demonstrated physiological effects with acupuncture. In one study, needling bladder points located on the foot (purported to treat visual disorders) was associated with changes in MRI signals at the visual cortex [160]. Multiple other acupuncture-MRI studies have also shown effects [161-165].

1.2.5.1.3. Connective tissue and mast-cell degranulation

Another theory is that acupuncture points are associated with anatomic locations of loose connective tissue. A study that looked at points and meridians in the arm concluded that such an association was present. It is possible that such an association might relate to the concept of "grasp" noted by practitioners. It has been proposed that acupuncture needling elicits mast-cell degranulation [163-177].

1.2.5.1.4. Acupuncture clinical application

There have been hundreds of controlled trials of acupuncture for various conditions.

Conditions for which acupuncture has been studied and appears to have possible efficacy (whether or not it has greater efficacy than sham acupuncture) include: chronic pain [178 - 181], postoperative nausea and vomiting [182], chemotherapy induced nausea [183-185], acute pain including dental pain [186-197], headache [198-204], hypertension [205]. Acupuncture has been studied for many other conditions including stroke [206-210], depression [211], fibromyalgia [212, 213], and tobacco use [214, 215], but the evidence is insufficient to recommend the use of acupuncture for these conditions.

1.2.5.1.5. Acupuncture-related adverse events

Acupuncture is generally safe, but can lead to the complications seen with any type of needle use. These include transmission of diseases, needle fragments left in the body, nerve damage, pneumothorax, pneumoperitoneum, organ puncture, cardiac tamponade, and osteomyelitis [216, 217]. Local complications include bleeding, contact dermatitis, infection, pain, and paresthesias [218]. Despite the variety of listed complications and the occasional case reports in major journals [219-222], major adverse events are exceedingly rare and are usually associated with poorly trained unlicensed acupuncturists [223]. A prospective study in Japan of 65,482 acupuncture treatments reported no major adverse events [224-227]. A prospective investigation in Germany of 97,733 patients constituting 760,000 treatment sessions reported that the two most frequently reported adverse events were needling pain (3.3%) and hematoma (3.2%) [228]. Potentially serious adverse events included two cases of pneumothorax. An asthma attack, a vasovagal reaction, an acute hypertensive crisis, and an exacerbation of depression were considered to be possibly related to treatment. Another two surveys performed in the United Kingdom totaling 66,000 treatments reported no serious adverse events [228, 229].

In general, local contraindications to acupuncture include active infection at insertion sites as well as malignancy at such sites, since there is a theoretical risk of causing metastatic dispersal of tumor cells [230].
Electroacupuncture should generally be avoided in patients with an automatic implantable cardioverter-defibrillator (AICD) or pacemaker [231].
Any disruption of the skin should be avoided in patients with severe neutropenia as seen after myelosuppressive chemotherapy [232].
Pregnancy is not an absolute contraindication, since acupuncture has been used and

studied for gestational conditions such as breech presentation and pregnancy-associated nausea. According to acupuncture theory, however, some points can induce labor, and the acupuncturist should be informed of the pregnancy [233-242].
Bleeding disorders and use of anticoagulants are also not absolute contraindications [243]. Acupuncture needles are nearly always thinner than the intravenous catheters or phlebotomy needles routinely administered in hospitals. The acupuncturist should be notified of any bleeding risks. In summary: acupuncture is considered very safe if rates of adverse effects are compared to those seen in many pharmacologic treatments. Practitioners should use sterile needles to prevent transmission of disease. In the US, acupuncture practitioners are required to use disposable sterile needles.

1.2.5.2. Challenges in acupuncture research: the issue of good control, placebo effect, and point specificity

A consensus conference sponsored by the National Institutes of Health in 1997 suggest that more research needs to be conducted to fully understand the biological actions and the clinical efficacy of acupuncture [244]. This conclusion was reinforced in the executive summary of a special report stemming from a workshop in 2001 examining the state of complementary and alternative medicine in cardiovascular, lung and blood research [245]. There have been more than 500 randomized controlled clinical trials in acupuncture over the last 30 years [246]. A randomized controlled trial should be hypothesis driven, prospective, blinded (preferably double blinded), adequately powered with sufficient numbers of subjects, well controlled and analyzed using appropriate statistical methodology. Additionally, description of the randomization process and dropouts should be provided. Many of these issues have not been adequately addressed in previous clinical acupuncture research [247]. Some of the problems encountered with acupuncture randomized trials are shared by trials in many domains: inadequate sample size, lack of follow up, imprecise outcomes, improper statistical analysis, and others. Some problems, however, are particular to acupuncture research. Issues include: Identifying an acupuncture treatment for a biomedical defined disease can be difficult.

One disease in biomedicine can represent many "patterns" within the Eastern medicine classification schema[248]. As an example, diabetes can have Eastern medical diagnoses of "stomach fire", "kidney fire", or "lung fire" [112]. Individualized treatments seen in acupuncture run counter to the standardized treatments used in randomized trials.

Researchers have tried to deal with this by performing pragmatic trials (where acupuncturists are given full freedom) or trials using semi standardized treatment (where acupuncturists are assigned mandatory points but given additional individualized options). Whether this latter approach approximates real acupuncture treatments is uncertain, as few studies have reported on the acupuncturists' perceptions of whether their treatments were constrained.

Acupuncture entails many different styles and techniques. In the United States alone, at least eight different styles of acupuncture are taught in the various accredited schools. Differences exist on what points are to be needled, how the needle should be manipulated, how long the needle should be kept in, and what is the appropriate response elicited from the patient. Thus it is difficult to know whether the results of a trial of single type of acupuncture can be generalized to other types. [249-254]

Due to the heterogeneity of acupuncture, an optimal control for one style may not be ideal for another. It is difficult to perform a double-blind acupuncture study. Acupuncturists are typically able to distinguish real treatment from sham treatment. Delivering acupuncture is not as simple as administering pills, and much like psychotherapy and surgery, experience may play a critical role in determining outcome.

Although acupuncture may provoke beneficial effects, several aspects need to be addressed regarding clinical trials with acupuncture [255, 256]. First, it is difficult to blind subjects and almost impossible to blind the therapist. If patients have any previous experience with acupuncture, they will already expect a sensation of de qi. It has been shown that acupuncture is likely to be most beneficial in patients who have high expectations of benefit [257]. Additionally, it is not possible to avoid the interaction between the therapist and the patient, and this is the basis of many placebo responses (the Rosenthal Effect) [258]. One possible solution is to select subjects that are acupuncture-naive, and to confirm that there is a feeling associated with the needling (de qi), Also, individuals performing data analysis should be blinded to the intervention.

Criticism of prior acupuncture studies include a lack of objective endpoints and inadequate or absent controls [259]. In studies addressing acupuncture in human subjects, different types of experimental controls have been described in the literature:

False acupuncture (sham) in which the needle guide-tube is applied without the needle, simulating the touch of the needle on the skin [260]; inserting a guide-tube with a toothpick inside; using a needle that recoils without touching the skin (placebo needle of

Streitberger) [261, 262].

Needling points on the skin not considered to be acupuncture points, also called “non-acupoints” or “dummy points” [260, 263, 264]. However, non-acupoint acupuncture has been shown to have analgesic effects in up to 50% of study patients ([265]

Superficial needling [266]. Needling of non-acupuncture points with minimal stimulation, an “invasive sham” acupuncture procedure ([267]. However, both minimal acupuncture and the placebo acupuncture with the sham acupuncture needle touching the skin evoke activity in cutaneous afferent nerves. This afferent nerve activity has pronounced effects on the functional connectivity in the brain resulting in a 'limbic touch response'.

Clinical studies have shown that both acupuncture and minimal acupuncture procedures induced significant alleviation of migraine and that both procedures were equally effective. In other conditions such as low back pain and knee osteoarthritis, acupuncture was found to be more potent than minimal acupuncture and conventional non-acupuncture treatment. It is probable that the responses to 'true' acupuncture and minimal acupuncture are dependent on the etiology of the pain. Furthermore, patients and healthy individuals may have different responses. As such, some authors argue that minimal acupuncture is not valid as an inert placebo-control despite its conceptual brilliance[268].

Needling in the same “meridian” of the experimental acupoint or in other acupoints on the same meridian of the experimental point which is considered to be “inactive” to the aimed effect. [269].

Laser acupuncture, in which the control refers to turning off the laser. [270, 271].

Control without any treatment or placebo tablet [264].

Needling without manual or electrical stimulation [247].

Recently, experimental studies have shown that insertion of a needle without manipulation or electrical stimulation does not activate afferent pathways and hence does not provide information to the central nervous system [247]. In the absence of any information transmitted to the CNS, any response would have to a placebo effect.

Mayer (2000) reviewed a number of acupuncture studies in treatment of pain and nausea and vomiting and made a convincing argument that the strongest control is to perform acupuncture along a meridian at an inactive acupoint or in the same segment outside a meridian, but that simply tapping the skin with a needle to stimulate acupuncture constitutes a weak control [272]. However this consideration brings up the concept of point specificity. which states that separate physiological and clinical responses result from stimulation of different acupoints, with some acupoints causing a profound response

and others causing a small or no response at all [273]. Clearly, acupuncture‟s success derives, in part, from a practitioner‟s ability to stimulate the best single or best combination of acupoints for a particular condition.
It is important to control for placebo responses since acupuncture, like most medical therapies, can be associated with clinical responses simply by virtue of a nonspecific interaction between the therapist and the patient [275, 272].

1.2.5.3. Acupuncture's stimulation modality: manual versus electroacupuncture

Acupuncture can be stimulated either manually by simply inserting a needle in an acupuncture point, then either leaving it in place or twisting and thrusting the needle, until a sensation of dullness, warmth, fullness, tingling or aching in the tissue is achieved (the de qi feeling). The acupuncturist may sense the needle being grasped or tugged ("like a fish biting the hook") [276].

Electroacupuncture consists of stimulating the needles with a small amount of electrical current at low frequency (2 to 4 Hz) or high frequencies (100-200Hz) [277, 278]. Acupuncture points can also be stimulated by heat, pressure, laser light [298] and shockwaves [279]. While manual acupuncture (MA) has been practiced for almost 3000 years, electroacupuncture (EA) has been introduced more recently and it appears to be the strongest form of acupuncture [155], inducing a long clinical response in rats lasting from 1 to 12 h [280] according to animal experiments. These responses have led to treatment regimens of 30 to 45 min of acupuncture administered two to three times per week for 2 to 4 weeks. In experimental protocols, EA has the advantage over manual acupuncture since it is measurable and reproducible, and it allows a continuous and stable stimulation for any period of time [155, 281]. Many practitioners use manual acupuncture at several acupoints including acupoints within the same spinal segment, called "segmental acupuncture," or a combination of segmental and distant acupoints (i.e., auricular acupuncture). In the treatment of pain, there are numerous variations of these techniques, including inserting needles at myofascial trigger points and at the specific site of pain [282]. In general, diverse studies show that Acupuncture is effective for chronic pain :

In 2009, the National Health Service of the United Kingdom wrote in their low back pain clinical management guideline that for early management of persistent non-specific low

back pain, “an exercise programme, a course of manual therapy, or a course of acupuncture” should be recommended at the early stage.[283] In addition, trials on neck pain, headache, and osteoarthritis in the knee have all shown that acupuncture not only reduces pain but also improves patients’ physical function in the long term.

CHAPTER TWO

Clinical Research Protocol

2. Clinical Research Protocol

The Influence of Acupuncture on Pain Intensity and Grip Strength in Symptomatic Rhizarthrosis – a prospective, non-blinded, randomized clinical study with waiting list control

2.1. Academic and medical background

This clinical research project was developed as part of the Master Programme in Traditional Chinese Medicine (TCM) of the Abel Salazar Institute of Biomedical Sciences – University of Porto (ICBAS-UP), 2012-2014th edition.
The research will be performed in order to obtain the Masters degree in TCM by the student Christiane Grünecker, main researcher of the current project.

Rhizarthrosis remains a difficult pathology for the treatment through Western medicine therapeutical strategies.
As a governement licensed German naturopath and student of TCM, the main interest of the author is to evaluate the possible benefit of integrating acupuncture into the conventional treatment of Rhizarthrosis.

2.2. Background

The trapeziometacarpal joint (TMC) is a specialized saddle-shaped joint, that allows the thumb to have a wide range of motions, including up, down, across the palm, and the ability to pinch. The thumb accounts for up to 40% of hand function and the functional importance of this joint explains that any pathological process that changes it could lead to chronic social and occupational disability and have significant repercussions on everyday activities.

2.2.1. Study-Focus Rhizarthrosis

To the present date, we have found no reliable published studies on acupuncture for Rhizarthrosis. Given the biological plausibility of acupuncture's effects and its clinical good outcomes already shown for other pathologies, it may be possible that acupuncture has beneficial effects on this pathology. However, this hypothesis has yet to be

scientifically corroborated.

Rhizarthrosis appears in postmenopausal women after the age of 50 in more than 30% of women. It is ten times more frequent in women than in men. The etiology is multifactorial and the exact mechanism is unknown. Frequent symptoms are: pain at the base of the thumb, difficulty with tasks (such as opening jars, turning a key), stiffness of the thumb, hyperextension of the middle thumb joint, pain at rest and pain during the night.

Eaton and Glickel described the radiographic severity of basilar joint arthritis, and these stages are often used to dictate treatment. Restoration of thumb function with a pain-free, stable, and mobile joint with preserved strength are the main goals of treatment of painful arthritis of the thumb.

Conservative measures to address symptoms include oral anti-inflammatory medications, activity modification and splinting, and intraarticular corticosteroid injections. Surgical treatment of rhizarthrosis is indicated in progression of the symptoms and increase of functional restriction despite conservative treatment

Surgical interventions include beak ligament reconstruction, arthroscopic synovectomy, arthroplasty, and finally arthrodesis of the affected articulations. Although short-term results from synovectomy and arthroplasty seem promising, long-term data are not yet available. Several surgical measures are available to us and require differentiated establishment of the indication. Trapezectomy with and without tendon interposition enables an improvement of symptoms. However, the increasing shortening of the thumb and the weakness and limitation to movement associated with this is to be regarded as disadvantageous. Arthrodesis of the metacarpophalangeal and interphalangeal joints yields a stable yet functional thumb with reliably good pain relief.

2.3. Justification of the study

Despite the conventional medical and surgical treatments, in many cases of rhizarthrosis, neither conservative treatment nor standard surgical techniques can successfully solve all the symptoms. Overall, the results of conventional treatments are many times unsatisfactory to patients that remain with pain and limitations in their daily life activities.

Acupuncture has effects on pain relief for different musculoskeletal diseases (e.g. back pain; osteoarthritis of the knee) and its analgesic mechanisms are well studied. The present state of the scientific evidence of acupuncture is such that is has in fact been approved as a “medical competence” by the Portuguese Medical Association since 2002.

2.4. Research team

2.4.1. Main investigators

Christiane Gruenecker
Government Licenced Naturopath (Germany). Student of the Master in Traditional Chinese Medicine – ICBAS, UP.

Nuno Correia
Specialist in Internal Medicine – Serviço de Urgência, Hospital São João, Centro Hospitalar São João, Porto. Master in Traditional Chinese Medicine at Abel Salazar Institute for Biomedical Sciences
Invited Assistent Professor of General Pathology – Escola Superior de Enfermagem, Universidade do Porto.

2.4.2. Research supervisors

Main supervisor: Prof. Doutor Henry Johannes Greten. Director of the TCM Master Programme – ICBAS, UP. Head of the Heidelberg School of Traditional Chinese Medicine; President of the German Society of Traditional Chinese Medicine (DGTCM), Heidelberg, Germany.

Co-supervisor: Prof. Doutor Jorge Machado – Director of Physiology Laboratory and Co-director of TCM Master Programme, ICBAS-UP.

2.5. Study hypothesis

Will acupuncture improve grip strength in patients with chronic pain in the trapeziometacarpal joint including patients with symptomatic rhizarthrosis ?

2.6. Methods

2.6.1. Study population

This study focuses on patients between 40 and 90 years-old with symptomatic Rhizarthrosis Eaton Stage <3.

2.6.2. Study design

Prospective, randomized, non-blinded clinical study with waiting list control .

2.6.3. Randomization to intervention groups

The selected 38 patients will be randomly assigned to the experimental (intervention) group or control (waiting list) group by the method of the coin flip.

2.6.4. Outcomes and measurements

2.6.4.1. Main outcomes

Pain intensity: as evaluated by Visual Analogue Scale (0-10)
Grip strength: as measured by a Martin Vigorimeter

Fig. 12 The Martin Vigorimeter

2.6.4.2. Secondary Outcomes

Daily activities and pain will be assessed with the “Disabilities of the Arm, Shoulder and Hand Questionnaire (DASH score).

2.6.5. Eligibility criteria

Inclusion criteria: diagnosis of Rhizartrosis of Eaton Stage <3, age over 18 years, no surgery ,no steroid injection, no change of medication during the study; informed consent.
Exclusion criteria: Under anticoagulant treatment; under medication with glucocorticoids or immune suppressives, chronic polyarthritis, rheumatoid arthritis and other rheumatologic diseases, intra-articular injection of steroids in the 3 months before study.
Rhizarthrosis = Eaton Stage < 3

2.6.6. Sampling and recruitment procedures

A convenience sample will be selected based on the review of clinical files of patients with Rhizarthrosis Eaton Stage <3 and listed according to eligibility criteria. The main researchers will contact the potential participants, explaining the study, asking questions regarding eligibility requirements and inviting them to participate. On the first day, subjects will sign the written informed consent.

2.6.7. Experimental procedures

Intervention group is submitted to 4 sessions of manual acupuncture during 2 weeks.
Pain intensity, Grip strenght will be measured before and after each session of acupuncture. DASH is evaluated before and after the two intervention weeks.
Follow-up : 12 patients of the interventiongroup are submitted to a third measurement of VAS and Grip two weeks after end of treatment, in order to evaluate the washout effect of the suppletive needling technique.
Control group: continues with usual care without any medical intervention while being in the waiting list control group for two weeks.
Pain evaluation (VAS) DASH and the grip strength measuring will be assessed in the beginning and at the end of the two weeks.

Acupuncture points and technique :

The selection of acupuncture points is based on potential local and segmental effects:

Lung= Pulmo = P

P9 = vorago major

P 10 = linea piscis

P 5extra (heidelberg Model)

IntestinumCrassum = IC

IC 10 = vicus tertius manus

IC 4 = valles conjuntae

Extrapoint on the hand

EX 14 octo heteropathias

thumbsides

Suppletive manual acupuncture will be performed with rotation of the needles until a sensation of “DeQi” is attained.

Sample: n= 38 adults

Interventiongroup: n=38 (33 female), 46-75 y.o, submitted to acupuncture, 4 sessions in 2 weeks.

Waitinglist controlgroup: n = 15 (13 female), 46-75 y. were assessed before and after two weeks while standing by

Followup group: n=12 (10 female) 46 -75 y, randomizly recruited from Interventiongroup. In order to get an idea of the possible further evolution of symptoms, and thereby evaluate the needed wash-out period for future cross-over studies, comparing suppletive acupuncture to bloodletting acupuncture (Leopard spot technique of the HeidelbergModel of TCM) one more series of measurements of the parameters VAS and Grip Strength were taken two weeks after completion of treatments .

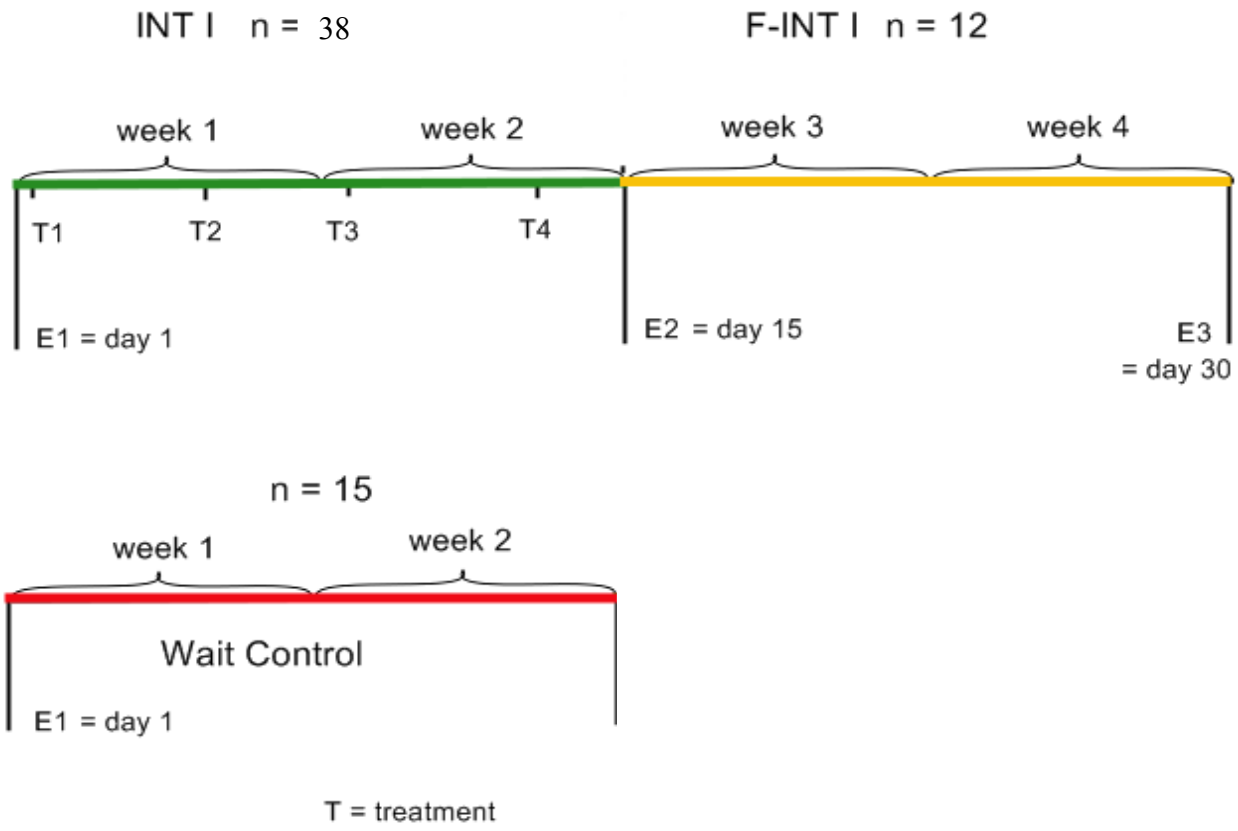


Fig. 13 Schematic representation of the experiment set-up

2.6.7.1. Intervention

Patients were treated with classical suppletive acupuncture in a sequence of four treatments in two weeks. The selection of acupuncture points was based on potential local and segmental effects as supposed in "the Heidelberg Model of Traditional ChineseMedicine".

Manual acupuncture was performed with rotation of the needles until a sensation of numbness („DeQi“) occurred.

The Interventiongroup was subject to four treatments in two weeks

2.6.7.2. Measurements

Before and after the treatments, measurements were taken by: DASH (Disability of Arm, Shoulder and Hand), VAS (visual analog scale) and grip strength (evaluation by means of a Martin vigorimeter).

2.6.8. Statistical plan

Results from this prospective clinical study will allow an accurate estimation of power calculations and sample size for a subsequent clinical trial since statistical data from previous studies is scarce.

2.6.9. Financial Issues

All material costs are supported by the researchers.

2.6.10. Ethical considerations, protection of human subjects and assessment of safety

All subjects for this study will be provided with a consent form describing this study and providing sufficient information for subjects to make an informed decision about their participation in this study. Subjects are informed about the goals, methods, expected benefits, and potential risks or discomforts, and have the right to decide to withdraw or continue at any moment during his/her participation. The subject is also aware that no prejudice will result if he/she refuses to participate or withdraws from the study.

This informed consent is obtained from all participants before randomization and is considered an inclusion criteria. This consent form has been approved by the EC and must be signed by the subject or legally acceptable surrogate and the investigator-designated research professional obtaining the consent.

There will be no interference or any change in patient's usual care and medication.

The incidence of adverse effects of acupuncture in multiple studies is low [228, 284-289].

Subjects will be asked about adverse experiences at each visit, defined as any unfavorable and unintended sign, symptom or disease temporally associated with the use of the acupuncture treatments.

Any adverse event that is life-threatening or results in death, hospitalization, a persistent or significant disability/incapacity, or cancer, will be promptly recorded and reported to the

Ethical Committee of ICBAS, Porto

The trial will be stopped if the investigators believe there is an unacceptable risk of serious adverse events in one of the treatment arms.

2.6.11. Expected results

It is expected that acupuncture treatments will reduce pain and improve grip in patients with Osteoarthrosis in the Trapeziometacarpaljoint.

This pilot study may lay ground for a future larger clinical trial with a randomized double-blinded controlled design in multicentric methodology. If acupuncture shows good results it may then be an additional therapeutic tool for the multidisciplinary treatment of this common disease.

CHAPTER THREE

Results

3. Results

Review of the recent literature indicates that acupuncture has effects on pain relief for different osteoarthrotic diseases and its analgesic mechanisms are well studied.
In the proposed study, patients of the intervention group experienced an improvement in DASH 44,51%, pain intensity improved in 40,54 %, grip strength improved 19,21 %
The follow-up group showed an improvement of VAS of 52, 85% in total and grip strength had and improvement of 16,62% (after four weeks,.two weeks intervention and two weeks follow-up without any intervention)
In the waiting-list group the difference was: 1,67 % increase in VAS, 1,18% reduction in Grip Strength and 1,25 increase % in Dash.

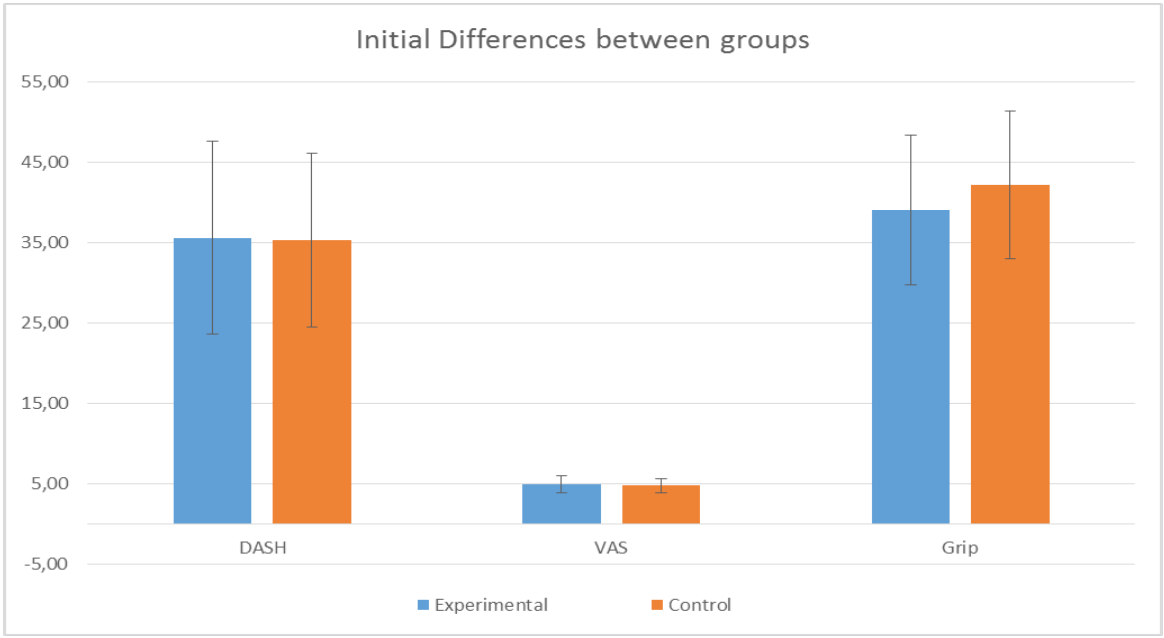


Fig. 14 Initial differences between intervention group and waiting list group

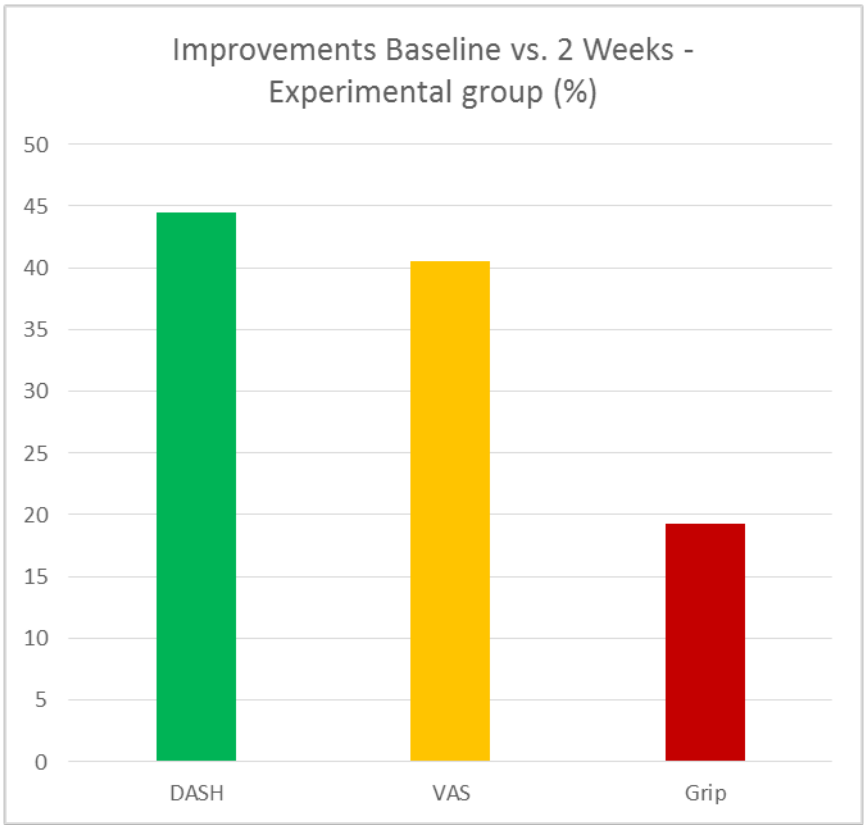


Fig. 15 Study results – Intervention group - improvement

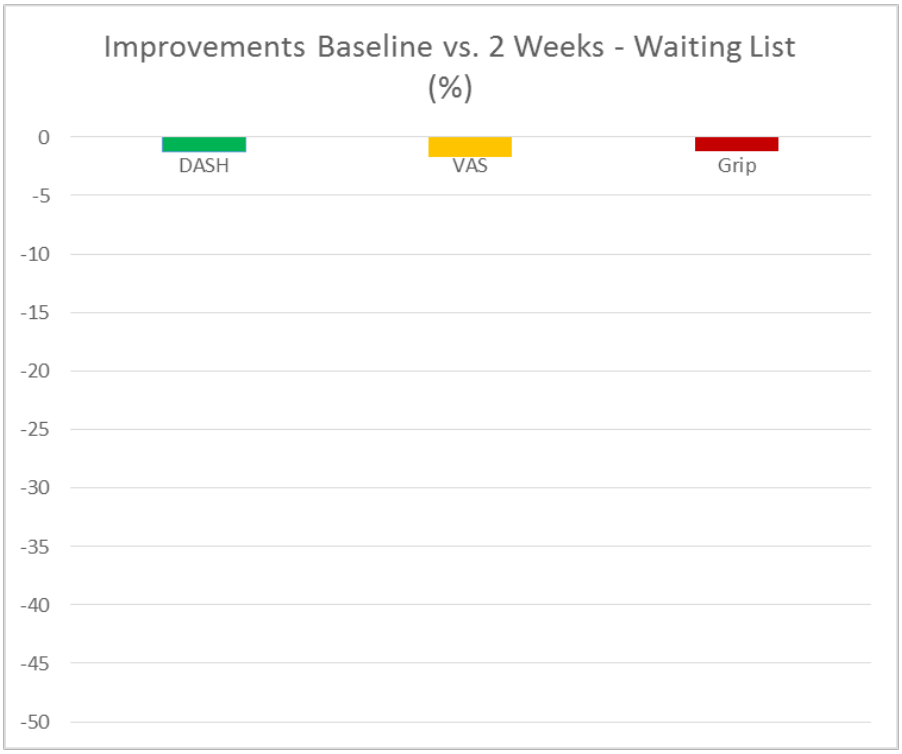


Fig. 16: Study results – Waiting list group - improvement

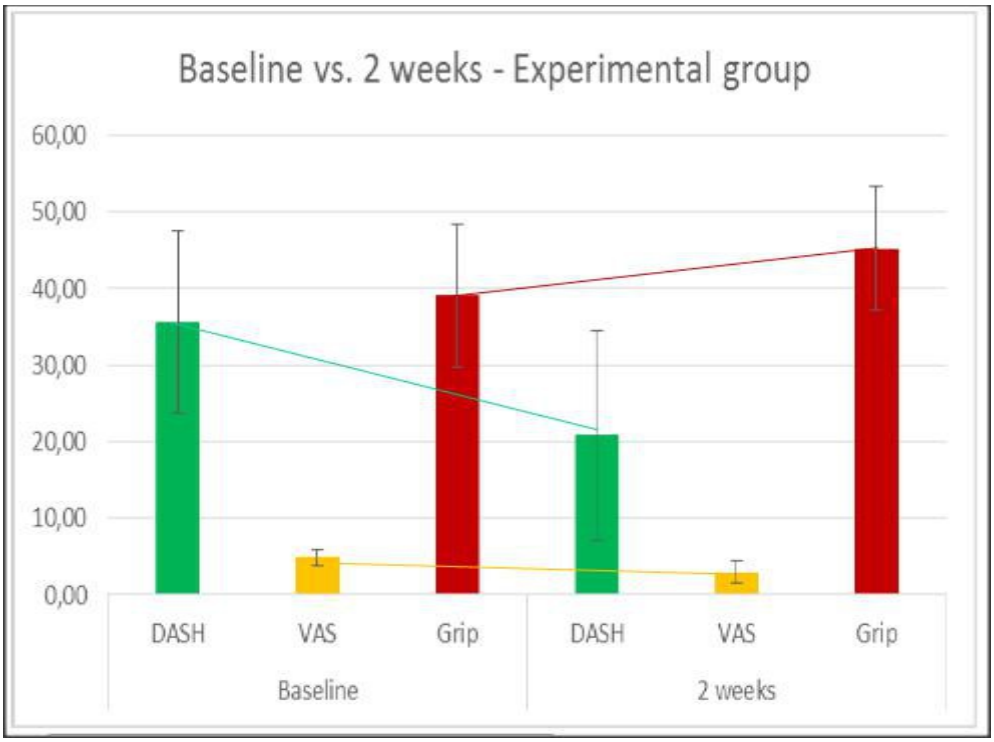


Fig. 17 Study results – Intervention group – evolution

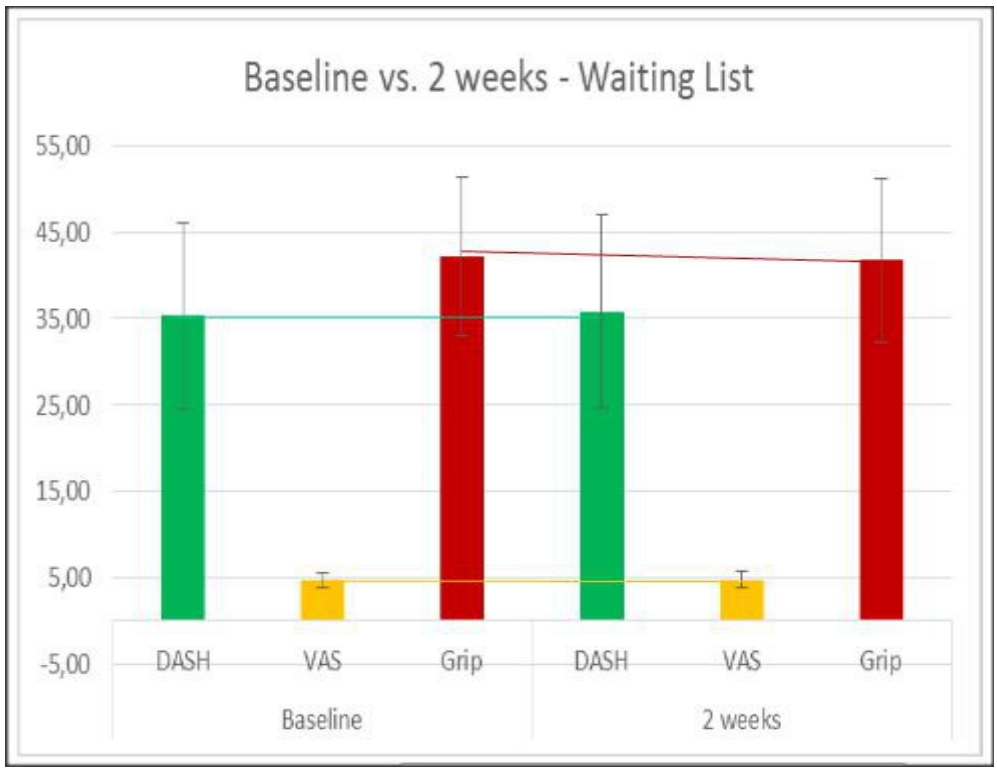


Fig. 18 Study results – Waiting list group - evolution

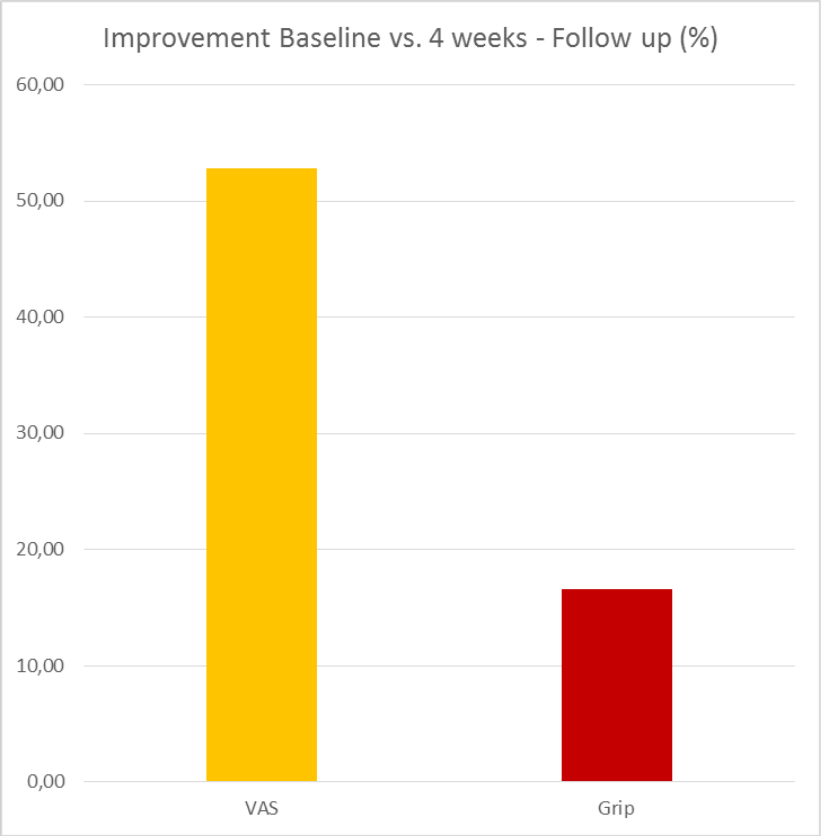


Fig. 19 Study results – Follow-up group – improvement baseline vs 4 weeks

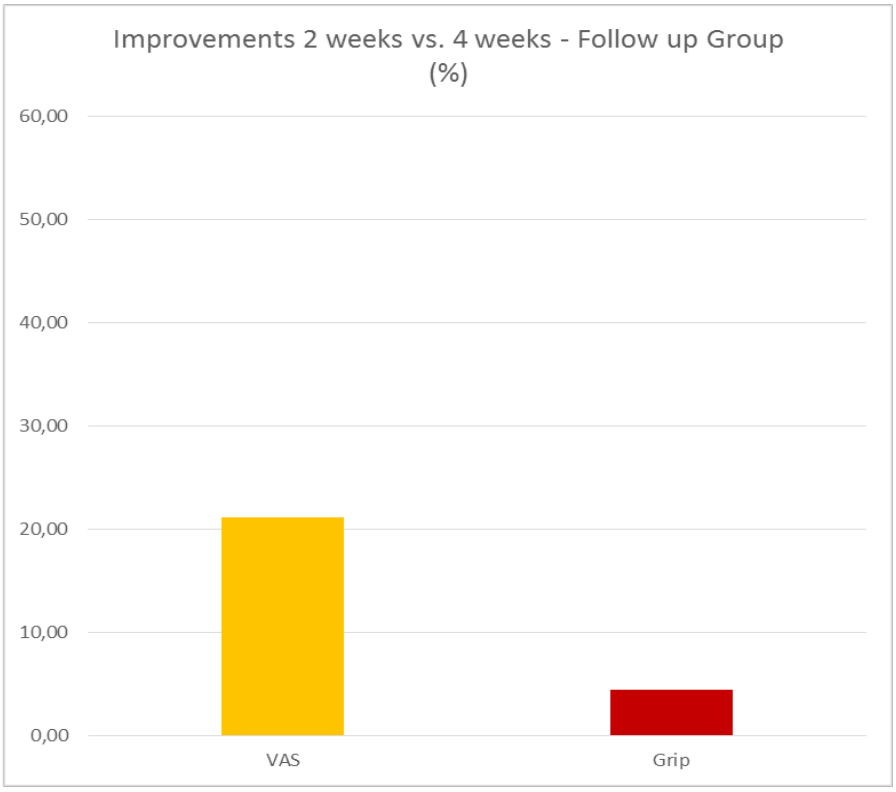


Fig. 20 Study results – Follow-up group – improvement 2 weeks vs 4 weeks

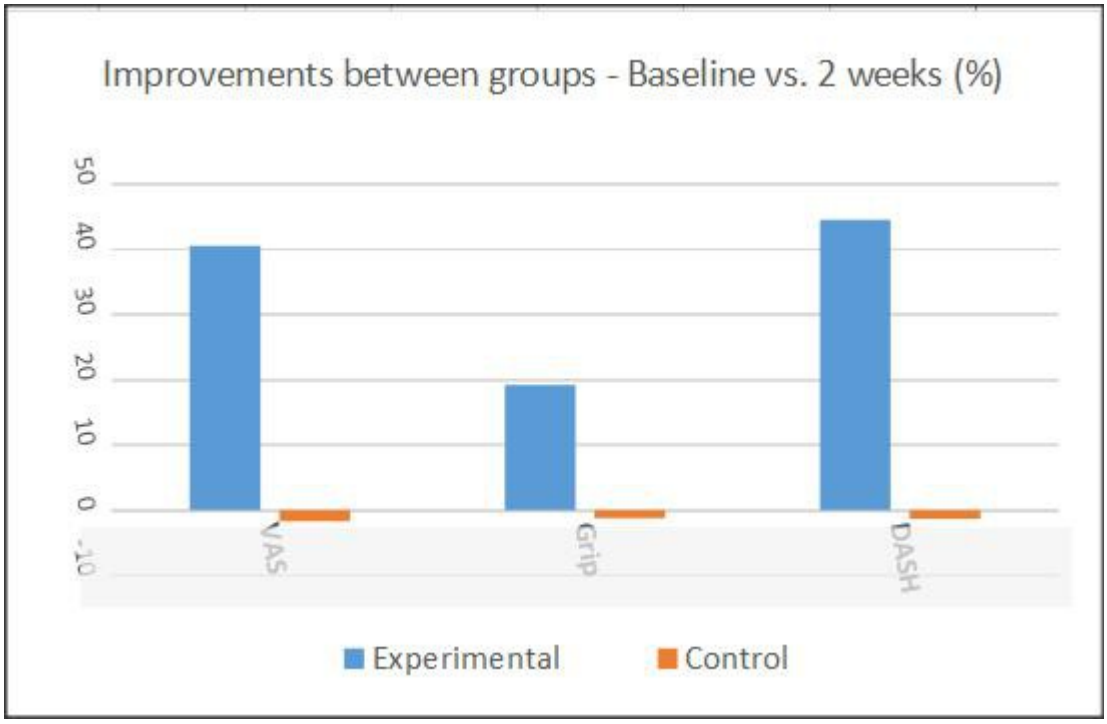


Fig. 21 Study results – improvements between groups – baseline vs 2 weeks

3.1 Conclusion

We found no reliable published studies on acupuncture for Rhizarthrosis (Ostoearthrosis of the Trapeziometacarpal joint)

Given the biological plausibility of acupuncture's effects and its clinical good outcomes already shown for other pathologies, it may be possible that acupuncture also has benificial effects on Rhizarthrosis.

The study suggests:

A:

The technique of suppletive needling seems to have a longer period of effect than expected.

In order to avoid a carry-over effect in a future possible clinical study with cross-over design, we suggest further studies with exact mesurement of the wash-out phase after suppletive needling.

A interesting follow-up study might be the compairing use of classical suppletive needling to the Leopard spot technique to relieve reactive calor in Rhizarthroses as proposed by The Heidelberg Model of TCM

B:

The results from the proposed prospective clinical study suggest that the effects of the chosen acupuncture points may be associated with a therapeutic benefit in the pathology of Rhizarthrosis

However, controversy persists whether the observed effects are specific to acupuncture or merely nonspecific consequences of needling.

Therefore, a future study could have the objective to determine the efficacy of different acupuncture treatment modalities. There could be compared verum and sham acupuncture (needling of non-specific points) in a prospective randomised trial with a double-blinded study design.

References

1) Bettinger PC, Linscheid RL, Cooney WP 3 rd , An KN (2001). Trapezial tilt: a radiographic correlation with advanced trapeziometacarpal joint arthritis. Journal of HandSurgery - American Volume. 26(4):692-7

2) Eaton RG, Glickel SZ, Littler JW (1985). Tendon interposition arthroplasty for degenerative arthritis of the trapeziometacarpal joint of the thumb. Journal of Hand Surgery - American Volume. 10(5):645-54

3) Gwynne-Jones DP, Penny ID, Sewell SA, Hughes TH (2006). Basal thumb metacarpal osteotomy for trapeziometacarpal osteoarthritis. Journal of Orthopaedic Surgery.14(1):58-63

4) Hobby JL, Lyall HA, Meggitt BF (1998). First metacarpal osteotomy for trapeziometacarpal osteoarthritis. Journal of Bone & Joint Surgery - British Volume. 80(3):508-12

5) Kapandji AI, Heim UF (2002). [Reorientation osteotomy of the trapezial saddle]. [French] L'osteotomie de reorientation de la selle trapezienne. Chirurgie de la Main.21(2):124-33

6) Kapandji TG, Kapandji AI (1993). [New radiologic data on the trapezo-metacarpal joint. The results of 330 cases]. [French] Nouvelles donnees radiologiques sur la trapezo-metacarpienne. Resultats sur 330 dossiers. Annales de Chirurgie de la Main et du Membre Superieur. 12(4):263-74

7) Pellegrini VD Jr (2005). The ABJS 2005 Nicolas Andry Award: osteoarthritis and injury at the base of the human thumb: survival of the fittest? Clinical Orthopaedics & Related Research. 438:266-76

8) Standring S (2008). Gray's Anatomy: The Anatomical Basis of Clinical Practice, 40th Edition. Churchill Livingstone Elsevier. P 857-898

9) Tomaino MM (2000). Treatment of Eaton stage I trapeziometacarpal disease with thumb metacarpal extension osteotomy. Journal of Hand Surgery - American Volume.25(6):1100-6 Vermeulen GM, Slijpe

10) Wilson JN, Bossley CJ (1983). Osteotomy in the treatment of osteoarthritis of the first carpometacarpal joint. Journal of Bone & Joint Surgery - British Volume. 65(2):179-81

11) Zancolli E (1979). Structural and Dynamic Bases of Hand Surgery, 2 nd Edition. J.B. Lippincott Company

12) Zancolli EA, Cozzi EP (1992). Atlas of Surgical Anatomy of the Hand. Churchill Livingstone.
13) Davis TR, Brady O, Dias JJ (2004). Excision of the trapezium for osteoarthritis of the trapeziometacarpal joint: a study of the benefit of ligament reconstruction or tendon interposition. J Hand Surg [Am]. Volume 29(6):1069-77
14) Lanzetta M, Foucher G (1995). A comparison of different surgical techniques in treating degenerative arthrosis of the carpometacarpal joint of the thumb. A retrospective study of 98 cases. Journal of Hand Surgery - British Volume. 20(1):105-10
15) Vermeulen GM, Slijper H, Feitz R, Hovius SE, Moojen TM, Selles RW (2011). Surgical management of primary thumb carpometacarpal osteoarthritis: a systematic review. J Hand Surg Am. 36(1):157-69.
16) Gomes Carreira AC, Jones A, Natour J. Assessment of the effectiveness of a functional splint for osteoarthritis of the trapeziometacarpal joint on the dominant hand: a randomized controlled study.J Rehabil Med 2010;42(5):469–74.
17) Meenagh GK, Patton J, Kynes C, Wright GD.A randomised controlled trial of intra-articular corticosteroid injection of the carpometacarpal joint of the thumb in osteoarthritis. Ann Rheum Dis 2004;63(10):1260–3.
18) Fuchs S, Monikes R, Wohlmeiner A, et al. Intra-articular hyaluronic acid compared with corticoid injections for the treatment of rhizarthrosis. Osteoarthritis Cartilage 2006;14:82–8 [PubMed].
19) Mandl LA, Hotchkiss RN, Adler RS, et al. Injectable hyaluronan for the treatment of carpometacarpal osteoarthritis: open label pilot trial. Curr Med Res Opin 2009;25(9):2103–8.
20) Figen Ayhan F, Ustün N. The evaluation of efficacy and tolerability of Hylan G-F 20 in bilateral thumb base osteoarthritis: 6 months follow-up. Clin Rheumatol 2009;28(5):535–41.
21) Stahl S, Karsh-Safriri I, Ratzon N, et al. Comparison of intra-articular injection of depot corticosteroids and hyaluronic acid for treatment of degenerative trapeziometacarpal joints. J Clin Rheumatol 2005;11:299–302 [PubMed].
22) Heyworth BE, Lee JH, Kim PD, et al. Hylan versus corticosteroid versus placebo for treatment of basal joint arthritis: a prospective, randomized, double-blinded clinical trial. J Hand Surg [Am] 2008;33: 40–8.
23) Grundberg AB, Reagan DS. Pathologic anatomy of the forearm: intersection syndrome. J Hand Surg 1985;10: 299–302.

24) Dobyns JH, Sim FH, Linscheid RL. Sports stress syndrome of hand and wrist. Am J Sports Med 1978;6:236–54.
25) Howard NJ. Peritendinitis crepitans. J Bone Joint Surg Br 1937;19:447–59.
26) Lee RP, Hatem SF, Recht MP. Extended MRI findings of intersection syndrome. Skeletal Radiol 2009;38(2):157–63.
27) Wood MD, Dobyns JH. Sports related extraarticular wrist syndrome. Clin Orthop Rel Res 1986;202:93–102
28) Palmer DH, Lane-Larsen CL. Helicopter skiing wrist injuries: a case report of 'bugaboo forearm.' Am J Sports Med 1994;22:148–9.
29) Servi JT. Wrist pain from overuse: detecting and relieving intersection syndrome. Phys Sports Med 1997;12: 41–4.
30) de Quervain F. Über eine Form von chronischer Tendovaginitis. Korresp Bl Schweiz Ärzte 1895;25:389.
31) de Quervain F. On a form of chronic tendovaginitis by Dr. Fritz de Quervain in la Chaux-de-Fonds. 1895. Am J Orthop 1997;26(9):641–4 (English translation of the original article).
32) Clarke MT, Lyall HA, Grant JW, Matthewson MH. The histopathology of de Quervain's disease. J Hand Surg 1998;23B(6):732–4.
33) Walker-Bone K, Palmer KT, Reading I, Coggon D, Cooper C. Prevalence and impact of musculoskeletal disorders of the upper limb in the general population. Arthritis Rheum 2004;51:642–51. doi: 10.1002/art.20535.
34) Le Viet D, Lantieri L. Ténosynovite de de Quervain. Cicatrice horizontale et fixation du lambeau capsulaire. Rev Chir Orthop Repar Appar Mot 1992;75(2):101–6.
35) Anderson SE, Steinbach LS, De Monaco D, et al. 'Baby wrist': MRI of an overuse syndrome in mothers. AJR Am J Roentgenol 2004;182(3):719–24.
36) Capasso G, Testa V, Maffulli N, et al. Surgical release of de Quervain's stenosing tenosynovitis postpartum: can it wait? Int Orthop 2002;26:23–5.
37) Armstrong ThJ, Fine LJ, Goldstein SA, et al. Ergonomic considerations in hand and wrist tendinitis. J Hand Surg 1987;12A:830.
38) Witczak JW, Mesear VR, Meyer RD. Triggering of the thumb with de Quervain's stenosing tendovaginitis.J Hand Surg 1990;15A(2):265
39) Albertson GM, High WA, Shin AY, Bishop AT. Extensor triggering in de Quervain's stenosing tenosynovitis. J Hand Surg 1999;24A(6):1311–4
40) Palmer K, Walker-Bone K, Linaker C, et al. The Southampton examination

schedule for the diagnosis of musculoskeletal disorders of the upper limb. Ann Rheum Dis 2000;59:5–11.
41) Pick RY. De Quervain's disease: a clinical triad. Clin Orthop Rel Res 1979;143: 165.
42) Weiss AP, Akelman E, Tabatabai M. Treatment of de Quervain's disease. J Hand Surg 1994;19A(4):595–8
43) Porkert M. The Theoretical Foundations of Chinese Medicine MIT Press; 1974.
44) Greten HJ. Kursbuch Traditionelle Chinesische Medizin. 2. ed. Stuttgart - New York: Thieme Publishing House 2006.
45) Liu Y. The Essential Book of Traditional Chinese Medicine: Theory, Clinical Practice: Columbia University Press 1988.
46) Greten HJ. Checkliste Chinesische Phytotherapie. 1. ed. Stuttgart - New York: Hippokrates Publishing House 2009.
47) Sivin N. Huang ti nei ching. Loewe M, Ed. Berkley and Los Angeles: University of California Press 1993.
48) http: //en.wikipedia.org/wiki/Traditional_Chinese_medicine. [09.10.09].
49) Kroenke K, Mangelsdorff AD. Common symptoms in ambulatory care: incidence, evaluation, therapy, and outcome. Am J Med 1989; 86(3): 262-6.
50) Ernst E. Acupuncture--how effective is it really? Fortschr Med 1998 20; 116(1-2): 20-6.
51) Ernst E. The risks of complementary therapy methods. Fortschr Med 1998 20; 116(1-2): 28-30.
52) White AR, Ernst E. A trial method for assessing the adequacy of acupuncture treatments. Altern Ther Health Med 1998; 4(6): 66-71.
53) Richardson J. The use of randomized control trials in complementary therapies: exploring the issues. J Adv Nurs 2000; 32(2): 398-406.
54) Bernstein BJ, Grasso T. Prevalence of complementary and alternative medicine use in cancer patients. Oncology (Williston Park) 2001; 15(10): 1267-72; discussion 72-8, 83.
55) Ashikaga T, Bosompra K, O'Brien P, Nelson L. Use of complimentary and alternative medicine by breast cancer patients: prevalence, patterns and communication with physicians. Support Care Cancer 2002; 10(7): 542-8.
56) WHO. www.who.int/mediacentre/factsheets/fs134/ en/. [08.10.09].
57) NIH. www.nccam.nih.gov/health/acupuncture/ introduction.htm. [08.10.09].
58) Sertel S, Herrmann S, Greten HJ, et al. Additional use of acupuncture to NSAID

effectively reduces post-tonsillectomy pain. Eur Arch Otorhinolaryngol 2009; 266(6): 919-25.

59) White AR, Filshie J, Cummings TM. Clinical trials of acupuncture: consensus recommendations for optimal treatment, sham controls and blinding. Complement Ther Med 2001; 9(4): 237-45.

60) Sertel S, Bergmann Z, Ratzlaff K, Baumann I, Greten HJ, Plinkert PK. Acupuncture for nasal congestion: A prospective, randomized, double-blind, placebo-controlled clinical pilot study. Am J Rhinol Allergy 2009 18.

61) Efferth T, Li PC, Konkimalla VS, Kaina B. From traditional Chinese medicine to rational cancer therapy. Trends Mol Med 2007; 13(8): 353-61.

62) Efferth T, Fu YJ, Zu YG, Schwarz G, Konkimalla VS, Wink M. Molecular target-guided tumor therapy with natural products derived from traditional Chinese medicine. Curr Med Chem 2007; 14(19): 2024-32.

63) Efferth T, Miyachi H, Bartsch H. Pharmacogenomics of a traditional Japanese herbal medicine (Kampo) for cancer therapy. Cancer Genomics Proteomics 2007; 4(2): 81-91.

64) Tang W, Hemm I, Bertram B. Recent development of antitumor agents from chinese herbal medicines; part I. Low molecular compounds. Planta Med 2003; 69(2): 97-108.

65) Tang W, Hemm I, Bertram B. Recent development of antitumor agents from Chinese herbal medicines. Part II. High molecular compounds(3). Planta Med 2003; 69(3): 193-201.

66) Newman DJ, Cragg GM. Natural products as sources of new drugs over the last 25 years. J Nat Prod 2007; 70(3): 461-77.

67) http: //www.who.int/mental_health/who_qol_field_trial_1995. WHOQOL. 1995 [08.10.09].

68) Browne JP, O'Boyle CA, McGee HM, et al. Individual quality of life in the healthy elderly. Qual Life Res 1994; 3(4): 235-44.

69) Lawton MP, Moss M, Glicksman A. The quality of the last year of life of older persons. Milbank Q 1990; 68(1): 1-28.

70) Development of the World Health Organization WHOQOL-BREF quality of life assessment. The WHOQOL Group. Psychol Med 1998; 28(3): 551-8.

71) Power M, Harper A, Bullinger M. The World Health Organization WHOQOL-100: tests of the universality of Quality of Life in 15 different cultural groups worldwide. Health Psychol 1999; 18(5): 495-505.

72) Wang GHH, Zang D. Quality of life of nurses in a general hospital. Chin Ment Health J 2001; 15(5): 308-11.

73) Norholm V, Bech P. The WHO Quality of Life (WHOQOL) Questionnaire: Danish validation study. Nord J Psychiatry 2001; 55(4): 229-35.

74) Fleck MP, Chachamovich E, Trentini C. Development and validation of the Portuguese version of the WHOQOL-OLD module. Rev Saude Publica 2006; 40(5): 785-91.

75) Ware JE, Jr., Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. Med Care 1992; 30(6): 473-83.

76) Ware JE, Jr, Kosinski M, Gandek B, et al. The factor structure of the SF-36 Health Survey in 10 countries: results from the IQOLA Project. International Quality of Life Assessment. J Clin Epidemiol 1998; 51(11): 1159-65.

77) Alonso J, Ferrer M, Gandek B, et al. Health-related quality of life associated with chronic conditions in eight countries: results from the International Quality of Life Assessment (IQOLA) Project. Qual Life Res 2004; 13(2): 283-98.

78) Leung KF, Liu FB, Zhao L, Fang JQ, Chan K, Lin LZ. Development and validation of the Chinese Quality of Life Instrument. Health Qual Life Outcomes 2005; 3: 26.

79) Wong W, Lam CL, Leung KF, Zhao L. Is the content of the Chinese Quality of Life Instrument (ChQOL) really valid in the context of traditional Chinese medicine in Hong Kong? Complement Ther Med 2009; 17(1): 29-36.

80) Schnyer RN, Conboy LA, Jacobson E, et al. Development of a Chinese medicine assessment measure: an interdisciplinary approach using the delphi method. J Altern Complement Med 2005; 11(6): 1005-13.

81) Trotti A, Johnson DJ, Gwede C, et al. Development of a head and neck companion module for the quality of life-radiation therapy instrument (QOL-RTI). Int J Radiat Oncol Biol Phys 1998 1; 42(2): 257-61.

82) Wong RK, Jones GW, Sagar SM, Babjak AF, Whelan T. A Phase I-II study in the use of acupuncture-like transcutaneous nerve stimulation in the treatment of radiation-induced xerostomia in head-and-neck cancer patients treated with radical radiotherapy. Int J Radiat Oncol Biol Phys 2003 1; 57(2): 472-80.

83) Juniper EF, Guyatt GH, Feeny DH, Ferrie PJ, Griffith LE, Townsend M. Measuring quality of life in children with asthma. Qual Life Res 1996; 5(1): 35-46. Patients Treated with Traditional Chinese Medicine The Open Otorhinolaryngology Journal, 2010, Volume 4 67

84) Stockert K, Schneider B, Porenta G, Rath R, Nissel H, Eichler I. Laser

acupuncture and probiotics in school age children with asthma: a randomized, placebo-controlled pilot study of therapy guided by principles of Traditional Chinese Medicine. Pediatr Allergy Immunol 2007; 18(2): 160-6.

85) Neumeister W, Kuhlemann H, Bauer T, Krause S, Schultze- Werninghaus G, Rasche K. Effect of acupuncture on quality of life, mouth occlusion pressures and lung function in COPD. Med Klin (Munich) 1999; 94(1 Spec No): 106-9.

86) Maille AR, Koning CJ, Zwinderman AH, Willems LN, Dijkman JH, Kaptein AA. The development of the 'Quality-of-life for Respiratory Illness Questionnaire (QOL-RIQ)': a disease-specific quality-of-life questionnaire for patients with mild to moderate chronic non-specific lung disease. Respir Med 1997; 91(5): 297- 309.

87) Pearman T. Quality of life and psychosocial adjustment in gynecologic cancer survivors. Health Qual Life Outcomes 2003; 1: 33.

88) Cassileth BR, Deng G. Complementary and alternative therapies for cancer. Oncologist 2004; 9(1): 80-9.

89) Dancey J, Zee B, Osoba D, et al. Quality of life scores: an independent prognostic variable in a general population of cancer patients receiving chemotherapy. The National Cancer Institute of Canada Clinical Trials Group. Qual Life Res 1997; 6(2): 151-8.

90) Efficace F, Bottomley A. Assessing HRQOL: a neglected issue for high-grade glioma. Lancet Oncol 2003; 4(1): 11-2.

91) Piao BK, Wang YX, Xie GR, et al. Impact of complementary mistletoe extract treatment on quality of life in breast, ovarian and non-small cell lung cancer patients. A prospective randomized controlled clinical trial. Anticancer Res 2004; 24(1): 303-9.

92) Chie WC, Lan CY, Chiang C, Chen CA. Quality of life of patients with ovarian cancer in Taiwan: validation and application of the Taiwan Chinese version of the EORTC QLQ-OV28. Psychoonco- logy 2009; Sept 23 [Epub ahead of print].

93) Oh B, Butow P, Mullan B, Clarke S. Medical Qigong for cancer patients: pilot study of impact on quality of life, side effects of treatment and inflammation. Am J Chin Med 2008; 36(3): 459-72.

94) Kaplan RM. Quality of life assessment for cost/utility studies in cancer. Cancer Treat Rev 1993; 19(Suppl A): 85-96.

95) Goldhirsch A, Gelber RD, Simes RJ, Glasziou P, Coates AS. Costs and benefits of adjuvant therapy in breast cancer: a quality-adjusted survival analysis. J Clin Oncol 1989 ; 7(1): 36-44.

96) Rusthoven JJ. Are quality of life, patient preferences, and costs realistic outcomes for clinical trials? Support Care Cancer 1997; 5(2): 112-7.

97) Feldstein ML. Quality-of-life-adjusted survival for comparing cancer treatments. A commentary on TWiST and Q-TWiST. Cancer 1991 1; 67(3 Suppl): 851-4.

98) Gelber RD, Goldhirsch A, Cavalli F. Quality-of-life-adjusted evaluation of adjuvant therapies for operable breast cancer. The International Breast Cancer Study Group. Ann Intern Med 1991 15; 114(8): 621-8.

99) Gelber RD, Goldhirsch A, Cole BF. Evaluation of effectiveness: Q- TWiST. The International Breast Cancer Study Group. Cancer Treat Rev 1993; 19 Suppl A: 73-84.

100) Gelber RD, Goldhirsch A, Cole BF, Wieand HS, Schroeder G, Krook JE. A quality-adjusted time without symptoms or toxicity (Q-TWiST) analysis of adjuvant radiation therapy and chemotherapy for resectable rectal cancer. J Natl Cancer Inst 1996 7; 88(15): 1039-45.

101) Stephens R. Clinically important differences in Q-TWIST - one twist too many? Qual Life Res 2006; 15(3): 425-6; discussion 7-8.

102) Jang RW, Le Maitre A, Ding K, et al. Quality-adjusted time without symptoms or toxicity analysis of adjuvant chemotherapy in non-small-cell lung cancer: an analysis of the National Cancer Institute of Canada Clinical Trials Group JBR.10 trial. J Clin Oncol 2009 10; 27(26): 4268-73.

103) Konkimalla VB, Efferth T. Evidence-based Chinese medicine for cancer therapy. J Ethnopharmacol 2008 5; 116(2): 207-10.

104) McCulloch M, See C, Shu XJ, et al. Astragalus-based Chinese herbs and platinum-based chemotherapy for advanced non-small- cell lung cancer: meta-analysis of randomized trials. J Clin Oncol 2006 20; 24(3): 419-30.

105) Pan CX, Morrison RS, Ness J, Fugh-Berman A, Leipzig RM. Complementary and alternative medicine in the management of pain, dyspnea, and nausea and vomiting near the end of life. A systematic review. J Pain Symptom Manage 2000 ; 20(5): 374-87.

106) Ezzo J, Vickers A, Richardson MA, et al. Acupuncture-point stimulation for chemotherapy-induced nausea and vomiting. J Clin Oncol 2005 1; 23(28): 7188-98. # Received: July 21, 2009 Revised: September 22, 2009 Accepted: September 25, 2009 © Sertel et al.; Licensee Bentham Open This is an open access article licensed under the terms of the Creative Commons Attribution Non-Commercial License (http: //creativecommons.org/licenses/by- nc/3.0/) which

permits unrestricted, non-commercial use, distribution and reproduction in any medium, provided the work is p. Patients Treated with Traditional Chinese Medicine The Open Otorhinolaryngology Journal, 2010, Volume 4 63

107) Haxsen, V., et al., Relevance of laser irradiance threshold in the induction of Alkaline phosphatase in human osteoblast cultures. Lasers Med Sci. 23(4), 2008, p. 381-4.

108) Litscher, G. and D. Schikora, Cerebral vascular effects of non-invasive laserneedles measured by transorbital and transtemporal Doppler sonography.Lasers Med Sci. 17(4), 2002, p. 289-95.

109) Litscher, G., et al., Acupuncture using laser needles modulates brain function: first evidence from functional transcranial Doppler sonography and functional magnetic resonance imaging. Lasers Med Sci. 19(1), 2004, p. 6-11.

110) Unschuld, P.U., Medicine in China : a history of ideas. Comparative studies of health systems and medical care. 1985, Berkeley: University of California Press xi, 423 p.

111) Ni, M., The Yellow Emperor's Classic of medicine : a new translation of the Neijing Suwen with commentary. 1st ed. 1995, Boston: Shambhala. xvi, 316 p.

112) Kaptchuk, T.J., The web that has no weaver : understanding Chinese medicine. [Rev. ed. 2000, Chicago, Ill: Contemporary Books. xxvi, 500 p.

113) Helms, J.M., Acupuncture energetics : a clinical approach for physicians. 1st ed. 1995, Berkeley, Calif., U.S.A.: Medical Acpuncture Publishers. xxiii, 759 p.

114) White, A. and E. Ernst, A brief history of acupuncture. Rheumatology (Oxford).43(5), 2004, p. 662-3.

115) Osler, W., The principles and practice of medicine : designed for the use of practitioners and students of medicine. 1892, New York: D. Appleton and Company. xvi, [2], 1079, [7], 8 p.

116) Reston, J., Now About My Operation in Peking, in New York Times 1971.

117) Birch, S.J. and R.L. Felt, Understanding acupuncture. 1999, Edinburgh ; New York: Churchill Livingstone. xv, 335 p.

118) Maciocia, G., The foundations of Chinese medicine : a comprehensive text for acupuncturists and herbalists. 1989, Edinburgh ; New York: Churchill Livingstone.xxiv, 498 p.

119) Greten, H., Kursbuch Traditionelle Chinesische Medizin. 2006: Thieme.

120) Porkert, M., Klinische chinesische Pharmakologie. 1978, Heidelberg: Verlag für Medizin Fischer. x, 630 p.

121) Porkert, M., The essentials of Chinese diagnostics. Fully rev. ed. 1983, Zürich, Switzerland Columbia, Md.: Chinese Medicine Publications ;Distributed in North America by Centre for Traditional Acupuncture. x, 292 p. (some folded).
122) Porkert, M., China, Konstanten im Wandel : moderne Interpretationen der chinesischen Klassik. 1. Aufl. ed. 1978, Stuttgart: S. Hirzel. x, 197 p.
123) Porkert, M., Lehrbuch der chinesischen Diagnostik. 1976, Heidelberg: Verlag für Medizin Fischer. 239 p.
124) Porkert, M., The theoretical foundations of Chinese medicine: systems of correspondence. M.I.T. East Asian science series,. 1974, Cambridge,: MIT Press. xvi, 368 p.
125) Porkert, M., Die theoretischen Grundlagen der chinesischen Medizin; das Entsprechungssystem. Münchener ostasiatische Studien, Bd. 5. 1973, Wiesbaden,: Steiner. 300 p.
126) Forschungsemeinschaft, D.-C., Scientifc approaches to Chinese Medicine. 2006, Heidelberg: Heidelberg School of Chinese Medicine.
127) Schroder, S., et al., Acupuncture treatment improves nerve conduction in peripheral neuropathy. Eur J Neurol. 14(3), 2007, p. 276-81.
128) Greten, H.J., Kick, A., Scholz, E., Fischer, J., Greten, T., Brazkiewicz, F., Schroder, S., Sertel, S., Acupuncture effects on heart failure: how to create objective study designs. J Acupunct Tuina Sci. 6, 2008 p. 307-308.
129) Greten, H.J., What is the role of Chinese Medical theory in modern scientific research. J. Acupunct. Tuina. Sci. 6(5), 2008, p. 259-260.
130) Sertel, S., et al., Additional use of acupuncture to NSAID effectively reduces post-tonsillectomy pain. Eur Arch Otorhinolaryngol. 266(6), 2009, p. 919-25.
131) Pomeranz, B., R. Cheng, and P. Law, Acupuncture reduces electrophysiological and behavioral responses to noxious stimuli: pituitary is implicated. Exp Neurol. 54(1), 1977, p. 172-8.
132) Pomeranz, B., Do endorphins mediate acupuncture analgesia? Adv Biochem Psychopharmacol. 18, 1978, p. 351-9.
133) Pomeranz, B. and D. Paley, Electroacupuncture hypalgesia is mediated by afferent nerve impulses: an electrophysiological study in mice. Exp Neurol. 66(2), 1979, p. 398-402.
134) Pomeranz, B. and N. Warma, Electroacupuncture suppression of a nociceptive reflex is potentiated by two repeated electroacupuncture treatments: the first opioid effect potentiates a second non-opioid effect. Brain Res. 452(1-2), 1988, p.

232-6.
135) Pomeranz, B. and R. Cheng, Suppression of noxious responses in single neurons of cat spinal cord by electroacupuncture and its reversal by the opiate antagonist naloxone. Exp Neurol. 64(2), 1979, p. 327-41.
136) Han, C.S., et al., The role of central 5-hydroxytryptamine in acupuncture analgesia. Sci Sin. 22(1), 1979, p. 91-104.
137) Han, J., et al., The role of central catecholamine in acupuncture analgesia. Chin Med J (Engl). 92(11), 1979, p. 793-800.
138) Han, J.S., Acupuncture analgesia. Pain. 21(3), 1985, p. 307-10.
139) Han, J.S., Recent progress in the study of acupuncture mechanisms. Zhen Ci Yan Jiu. 13(1), 1988, p. 36-42, 35.
140) Han, J.S., Acupuncture: neuropeptide release produced by electrical stimulation of different frequencies. Trends Neurosci. 26(1), 2003, p. 17-22.
141) Han, J.S., Acupuncture and endorphins. Neurosci Lett. 361(1-3), 2004, p. 258-61.
142) Han, J.S., et al., Central neurotransmitters and acupuncture analgesia. Am J Chin Med. 8(4), 1980, p. 331-48.
143) Liu, J.L., X.W. Han, and S.N. Su, The role of frontal neurons in pain and acupuncture analgesia. Sci China B. 33(8), 1990, p. 938-45.
144) Liu, D.M., et al., Physiologic effects of electroacupuncture combined with intramuscular administration of xylazine to provide analgesia in goats. Am J Vet Res. 70(11), 2009, p. 1326-32.
145) Chen, L., et al., Endogenous anandamide and cannabinoid receptor-2 contribute to electroacupuncture analgesia in rats. J Pain. 10(7), 2009, p. 732-9.
146) Chen, X.H., J.S. Han, and L.T. Huang, CCK receptor antagonist L-365,260 potentiated electroacupuncture analgesia in Wistar rats but not in audiogenic epileptic rats. Chin Med J (Engl). 107(2), 1994, p. 113-8.
147) Chen, X.H. and J.S. Han, Analgesia induced by electroacupuncture of different frequencies is mediated by different types of opioid receptors: another cross-tolerance study. Behav Brain Res. 47(2), 1992, p. 143-9.
148) Chen, X.H. and J.S. Han, All three types of opioid receptors in the spinal cord are important for 2/15 Hz electroacupuncture analgesia. Eur J Pharmacol. 211(2), 1992, p. 203-10.
149) Cheng, R.S. and B. Pomeranz, Monoaminergic mechanism of electroacupuncture analgesia. Brain Res. 215(1-2), 1981, p. 77-92.

150) Cheng, R.S. and B. Pomeranz, A combined treatment with D-amino acids and electroacupuncture produces a greater analgesia than either treatment alone; naloxone reverses these effects. Pain. 8(2), 1980, p. 231-6.
151) Cheng, R.S. and B.H. Pomeranz, Electroacupuncture analgesia is mediated by stereospecific opiate receptors and is reversed by antagonists of type I receptors. Life Sci. 26(8), 1980, p. 631-8.
152) Cheng, R.S. and B. Pomeranz, Electroacupuncture analgesia could be mediated by at least two pain-relieving mechanisms; endorphin and non-endorphin systems. Life Sci. 25(23), 1979, p. 1957-62.
153) Han, J.S. and L. Terenius, Neurochemical basis of acupuncture analgesia. Annu Rev Pharmacol Toxicol. 22, 1982, p. 193-220.
154) Andersson, S. and T. Lundeberg, Acupuncture--from empiricism to science: functional background to acupuncture effects in pain and disease. Med Hypotheses. 45(3), 1995, p. 271-81.
155) Ulett, G.A., S. Han, and J.S. Han, Electroacupuncture: mechanisms and clinical application. Biol Psychiatry. 44(2), 1998, p. 129-38.
156) Carlsson, C., Acupuncture mechanisms for clinically relevant long-term effects-reconsideration and a hypothesis. Acupunct Med. 20(2-3), 2002, p. 82-99.
157) Vickers, A.J., et al., Acupuncture of chronic headache disorders in primary care: randomised controlled trial and economic analysis. Health Technol Assess. 8(48), 2004, p. iii, 1-35.
158) Vickers, A., Acupuncture for treatment for chronic neck pain. Reanalysis of data suggests that effect is not a placebo effect. BMJ. 323(7324), 2001, p. 1306-7.
159) Change in the medical science of acupuncture, W.F.o.A.a.M. Societies, Editor. 1993: Kyoto.
160) Cho, Z.H., et al., New findings of the correlation between acupoints and corresponding brain cortices using functional MRI. Proc Natl Acad Sci U S A.95(5), 1998, p. 2670-3.
161) Fang, J.L., et al., Functional MRI in healthy subjects during acupuncture: different effects of needle rotation in real and false acupoints. Neuroradiology. 46(5), 2004, p. 359-62.
162) Fang, B. and J.C. Hayes, Functional MRI explores mysteries of acupuncture. Diagn Imaging (San Franc). 21(7), 1999, p. 19-21.
163) Wu, M.T., et al., Neuronal specificity of acupuncture response: a fMRI study with electroacupuncture. Neuroimage. 16(4), 2002, p. 1028-37.

164) Yan, B., et al., Acupoint-specific fMRI patterns in human brain. Neurosci Lett. 383(3), 2005, p. 236-40.
165) Yoo, S.S., et al., Modulation of cerebellar activities by acupuncture stimulation: evidence from fMRI study. Neuroimage. 22(2), 2004, p. 932-40.
166) Zhang, D., et al., Role of mast cells in acupuncture effect: a pilot study. Explore (NY). 4(3), 2008, p. 170-7.
167) Ahn, A.C., et al., Electrical impedance of acupuncture meridians: the relevance of subcutaneous collagenous bands. PLoS One. 5(7), p. e11907.
168) Napadow, V., et al., The status and future of acupuncture mechanism research. J Altern Complement Med. 14(7), 2008, p. 861-9.
169) Ahn, A.C., et al., Electrical properties of acupuncture points and meridians: a systematic review. Bioelectromagnetics. 29(4), 2008, p. 245-56.
170) Langevin, H.M., et al., Connective tissue fibroblast response to acupuncture: dose-dependent effect of bidirectional needle rotation. J Altern Complement Med. 13(3), 2007, p. 355-60.
171) Langevin, H.M., et al., Subcutaneous tissue fibroblast cytoskeletal remodeling induced by acupuncture: evidence for a mechanotransduction-based mechanism.J Cell Physiol. 207(3), 2006, p. 767-74.
172) Langevin, H.M., et al., Tissue displacements during acupuncture using ultrasound elastography techniques. Ultrasound Med Biol. 30(9), 2004, p. 1173-83.
173) Langevin, H.M. and J.A. Yandow, Relationship of acupuncture points and meridians to connective tissue planes. Anat Rec. 269(6), 2002, p. 257-65.
174) Langevin, H.M., et al., Evidence of connective tissue involvement in acupuncture. FASEB J. 16(8), 2002, p. 872-4.
175) Langevin, H.M., et al., Biomechanical response to acupuncture needling in humans. J Appl Physiol. 91(6), 2001, p. 2471-8.
176) Langevin, H.M., D.L. Churchill, and M.J. Cipolla, Mechanical signaling through connective tissue: a mechanism for the therapeutic effect of acupuncture. FASEB J. 15(12), 2001, p. 2275-82.
177) Langevin, H.M. and P.D. Vaillancourt, Acupuncture: does it work and, if so, how? Semin Clin Neuropsychiatry. 4(3), 1999, p. 167-75.
178) Manheimer, E., et al., Meta-analysis: acupuncture for osteoarthritis of the knee. Ann Intern Med. 146(12), 2007, p. 868-77.
179) Manheimer, E., et al., Meta-analysis: acupuncture for low back pain. Ann Intern

Med. 142(8), 2005, p. 651-63.
180) Furlan, A.D., et al., Acupuncture and dry-needling for low back pain: an updated systematic review within the framework of the cochrane collaboration. Spine (Phila Pa 1976). 30(8), 2005, p. 944-63.
181) White, P., et al., Acupuncture versus placebo for the treatment of chronic mechanical neck pain: a randomized, controlled trial. Ann Intern Med. 141(12), 2004, p. 911-9.
182) Streitberger, K., et al., Acupuncture compared to placebo-acupuncture for postoperative nausea and vomiting prophylaxis: a randomised placebo-controlled patient and observer blind trial. Anaesthesia. 59(2), 2004, p. 142-9.
183) Ezzo, J., K. Streitberger, and A. Schneider, Cochrane systematic reviews examine P6 acupuncture-point stimulation for nausea and vomiting. J Altern Complement Med. 12(5), 2006, p. 489-95.
184) Ezzo, J.M., et al., Acupuncture-point stimulation for chemotherapy-induced nausea or vomiting. Cochrane Database Syst Rev (2), 2006, p. CD002285.
185) Ezzo, J., et al., Acupuncture-point stimulation for chemotherapy-induced nausea and vomiting. J Clin Oncol. 23(28), 2005, p. 7188-98.
186) Smith, C.A., et al., Complementary and alternative therapies for pain management in labour. Cochrane Database Syst Rev (4), 2006, p. CD003521.
187) Smith, C.A. and C.A. Crowther, Acupuncture for induction of labour. Cochrane Database Syst Rev (1), 2004, p. CD002962.
188) Ernst, E. and M.H. Pittler, The effectiveness of acupuncture in treating acute dental pain: a systematic review. Br Dent J. 184(9), 1998, p. 443-7. 125
189) Rosted, P., et al., Acupuncture in the management of anxiety related to dental treatment: a case series. Acupunct Med. 28(1), p. 3-5.
190) Rosted, P., Acupuncture and gagging reduction during oral airway insertion. Anaesthesia. 64(7), 2009, p. 783-4; author reply 784.
191) Rosted, P., et al., The use of acupuncture in controlling the gag reflex in patients requiring an upper alginate impression: an audit. Br Dent J. 201(11), 2006, p. 721-5; discussion 715.
192) Rosted, P. and M. Bundgaard, Can acupuncture reduce the induction time of a local anaesthetic?--A pilot study. Acupunct Med. 21(3), 2003, p. 92-9.
193) Rosted, P. and V. Jorgensen, Acupuncture treatment of pain dysfunction syndrome after dental extraction. Acupunct Med. 20(4), 2002, p. 191-2.
194) Rosted, P., Practical recommendations for the use of acupuncture in the

treatment of temporomandibular disorders based on the outcome of published controlled studies. Oral Dis. 7(2), 2001, p. 109-15.
195) Rosted, P., Introduction to acupuncture in dentistry. Br Dent J. 189(3), 2000, p. 136-40.
196) Rosted, P., Use of acupuncture in dentistry. Aust Dent J. 43(6), 1998, p. 437.
197) Rosted, P., The use of acupuncture in dentistry: a review of the scientific validity of published papers. Oral Dis. 4(2), 1998, p. 100-4.
198) Ahn, A.C. and T.J. Kaptchuk, Advancing acupuncture research. Altern Ther Health Med. 11(3), 2005, p. 40-5.
199) Linde, K., et al., Acupuncture for migraine prophylaxis. Cochrane Database Syst Rev (1), 2009, p. CD001218.
200) Linde, K., et al., Randomized trial vs. observational study of acupuncture for migraine found that patient characteristics differed but outcomes were similar. J Clin Epidemiol. 60(3), 2007, p. 280-7.
201) Linde, K., et al., Treatment in a randomized multicenter trial of acupuncture for migraine (ART migraine). Forsch Komplementmed. 13(2), 2006, p. 101-8.
202) Linde, K., et al., Acupuncture for patients with migraine: a randomized controlledtrial. JAMA. 293(17), 2005, p. 2118-25.
203) Melchart, D., et al., Acupuncture versus placebo versus sumatriptan for early treatment of migraine attacks: a randomized controlled trial. J Intern Med. 253(2), 2003, p. 181-8.
204) Evans, R.W. and S.L. Linder, Management of basilar migraine. Headache. 42(5), 2002, p. 383-4.
205) Flachskampf, F.A., et al., Randomized trial of acupuncture to lower blood pressure. Circulation. 115(24), 2007, p. 3121-9. 126
206) Zhang, S.H., et al., Acupuncture for acute stroke. Cochrane Database Syst Rev(2), 2005, p. CD003317.
207) Wu, P. and S. Liu, Clinical observation on post-stroke anxiety neurosis treated by acupuncture. J Tradit Chin Med. 28(3), 2008, p. 186-8.
208) Xie, Y., et al., Acupuncture for dysphagia in acute stroke. Cochrane Database Syst Rev (3), 2008, p. CD006076.
209) Wu, H., et al., Acupuncture for Stroke Rehabilitation. Stroke, 2008.
210) Wu, H.M., et al., Acupuncture for stroke rehabilitation. Cochrane Database Syst Rev. 3, 2006, p. CD004131.
211) Smith, C.A. and P.P. Hay, Acupuncture for depression. Cochrane Database Syst

Rev (2), 2005, p. CD004046.
212) Ernst, E., Chiropractic treatment for fibromyalgia: a systematic review. Clin Rheumatol. 28(10), 2009, p. 1175-8.
213) Mayhew, E. and E. Ernst, Acupuncture for fibromyalgia--a systematic review of randomized clinical trials. Rheumatology (Oxford). 46(5), 2007, p. 801-4.
214) White, A.R., R.C. Moody, and J.L. Campbell, Acupressure for smoking cessation--a pilot study. BMC Complement Altern Med. 7, 2007, p. 8.
215) White, A.R., H. Rampes, and J.L. Campbell, Acupuncture and related interventions for smoking cessation. Cochrane Database Syst Rev (1), 2006, p. CD000009.
216) Lao, L., Acupuncture practice, past and present: is it safe and effective? J Soc Integr Oncol. 4(1), 2006, p. 13-5.
217) Lao, L., et al., Is acupuncture safe? A systematic review of case reports. Altern Ther Health Med. 9(1), 2003, p. 72-83.
218) Ernst, E. and A.R. White, Prospective studies of the safety of acupuncture: a systematic review. Am J Med. 110(6), 2001, p. 481-5.
219) Vucicevic, Z., et al., Multiloculated pleural empyema following acupuncture. Infection. 33(4), 2005, p. 297-8.
220) Saifeldeen, K. and M. Evans, Acupuncture associated pneumothorax. Emerg Med J. 21(3), 2004, p. 398.
221) Studd, R.C. and P.J. Stewart, Images in clinical medicine. Intraabdominal abscess after acupuncture. N Engl J Med. 350(17), 2004, p. 1763.
222) Cheng, T.O., Cardiac tamponade following acupuncture. Chest. 118(6), 2000, p. 1836-7.
223) Woo, P.C., et al., Acupuncture mycobacteriosis. N Engl J Med. 345(11), 2001, p. 842-3.
224) Yamashita, H. and H. Tsukayama, Safety of acupuncture. Incident reporting and feedback may reduce risks. BMJ. 324(7330), 2002, p. 170-1. 127
225) Yamashita, H., et al., Incidence of adverse reactions associated with acupuncture. J Altern Complement Med. 6(4), 2000, p. 345-50.
226) Yamashita, H., et al., Adverse events in acupuncture and moxibustion treatment: a six-year survey at a national clinic in Japan. J Altern Complement Med. 5(3), 1999, p. 229-36.
227) Yamashita, H., et al., Adverse events related to acupuncture. JAMA. 280(18), 1998, p. 1563-4.

228) Melchart, D., et al., Prospective investigation of adverse effects of acupuncture in 97 733 patients. Arch Intern Med. 164(1), 2004, p. 104-5.
229) MacPherson, H., et al., The York acupuncture safety study: prospective survey of 34 000 treatments by traditional acupuncturists. BMJ. 323(7311), 2001, p. 486-7
230) World Health Organization., Guidelines on basic training and safety in acupuncture. 1999, Geneva: World Health Organization. 30 p.
231) Lau, E.W., et al., Acupuncture triggering inappropriate ICD shocks. Europace. 7(1), 2005, p. 85-6.
232) Filshie, J., Safety aspects of acupuncture in palliative care. Acupunct Med. 19(2), 2001, p. 117-22.
233) van den Berg, I., et al., Cost-effectiveness of breech version by acupuncture-type interventions on BL 67, including moxibustion, for women with a breech foetus at 33 weeks gestation: a modelling approach. Complement Ther Med. 18(2), p. 67- 77.
234) Li, X., et al., Moxibustion and other acupuncture point stimulation methods to treat breech presentation: a systematic review of clinical trials. Chin Med. 4, 2009, p. 4.
235) Mitchell, M. and K. Allen, Breech presentation and the use of moxibustion. Pract Midwife. 11(5), 2008, p. 22-4.
236) Neri, I., et al., Effects of three different stimulations (acupuncture, moxibustion, acupuncture plus moxibustion) of BL.67 acupoint at small toe on fetal behavior of breech presentation. Am J Chin Med. 35(1), 2007, p. 27-33.
237) Cardini, F., et al., A randomised controlled trial of moxibustion for breech presentation. BJOG. 112(6), 2005, p. 743-7.
238) Neri, I., et al., Acupuncture plus moxibustion to resolve breech presentation: a randomized controlled study. J Matern Fetal Neonatal Med. 15(4), 2004, p. 247-52.
239) Neri, I., et al., Non-stress test changes during acupuncture plus moxibustion on BL67 point in breech presentation. J Soc Gynecol Investig. 9(3), 2002, p. 158-62.
240) Ewies, A. and K. Olah, Moxibustion in breech version--a descriptive review. Acupunct Med. 20(1), 2002, p. 26-9. 128
241) Ernst, E., Moxibustion for breech presentation. JAMA. 282(14), 1999, p. 1329; author reply 1329-30.
242) Cardini, F. and H. Weixin, Moxibustion for correction of breech presentation: a randomized controlled trial. JAMA. 280(18), 1998, p. 1580-4.

243) Sciammarella, J., Acupuncture in patients anticoagulated with warfarin. Medical Acupuncture. 13, 2002.
244) NIH Consensus Conference. Acupuncture. JAMA. 280(17), 1998, p. 1518-24.
245) Lin, M.C., et al., State of complementary and alternative medicine in cardiovascular, lung, and blood research: executive summary of a workshop. Circulation. 103(16), 2001, p. 2038-41.
246) Vickers, A.J., Bibliometric analysis of randomized trials in complementary medicine. Complement Ther Med. 6, 1998, p. 185-9.
247) Ernst, E. and A.R. White, A review of problems in clinical acupuncture research. Am J Chin Med. 25(1), 1997, p. 3-11.
248) Kaptchuk, T.J., Acupuncture: theory, efficacy, and practice. Ann Intern Med. 136(5), 2002, p. 374-83.
249) Barnes, L.L., American acupuncture and efficacy: meanings and their points of insertion. Med Anthropol Q. 19(3), 2005, p. 239-66.
250) Johnston, M.F., et al., Asian-American physicians distinguish between licensed acupuncturists and physicians who incorporate acupuncture into their practices. J Altern Complement Med. 10(6), 2004, p. 918-9.
251) Barnes, L.L., The acupuncture wars: the professionalizing of American acupuncture--a view from Massachusetts. Med Anthropol. 22(3), 2003, p. 261-301.
252) Diehl, D.L., et al., Use of acupuncture by American physicians. J Altern Complement Med. 3(2), 1997, p. 119-26.
253) Kantor, J.M., Acupuncture and herbalism on the American health care scene. Med Interface. 10(5), 1997, p. 95-8.
254) Brody, H., Chinese vs. American acupuncture. N Engl J Med. 287(14), 1972, p. 724-5.
255) Napadow, V., et al., The status and future of acupuncture clinical research. J Altern Complement Med. 14(7), 2008, p. 861-9.
256) Zhou, W. and J.C. Longhurst, Review of trials examining the use of acupuncture to treat hypertension. Future Cardiol. 2(3), 2006, p. 287-92.
257) Kalauokalani, D., et al., Lessons from a trial of acupuncture and massage for low back pain: patient expectations and treatment effects. Spine (Phila Pa 1976). 26(13), 2001, p. 1418-24
258) Rosenthal, R. and R.L. Rosnow, Artifacts in behavioral research : Robert Rosenthal and Ralph L. Rosnow's classic books : a re-issue of Artifact in

behavioral research, Experimenter effects in behavioral research and The volunteer subject. 2009, New York: Oxford University Press. xv, 886 p. 129
259) Hammerschlag, R., Methodological and ethical issues in clinical trials of acupuncture. J Altern Complement Med. 4(2), 1998, p. 159-71.
260) Middlekauff, H.R., Acupuncture inhibits sympathetic activation during mental stress in advanced heart failure patients. J Card Fail. 8, 2002, p. 399-406.
261) Kaptchuk, T.J., Placebo needle for acupuncture. Lancet. 352(9132), 1998, p. 992.
262) Streitberger, K. and J. Kleinhenz, Introducing a placebo needle into acupuncture research. Lancet. 352(9125), 1998, p. 364-5.
263) Wang, J.D., T.B. Kuo, and C.C. Yang, An alternative method to enhance vagal activities and suppress sympathetic activities in humans. Auton Neurosci. 100(1-2), 2002, p. 90-5.
264) Huang, S.T., et al., Increase in the vagal modulation by acupuncture at neiguan point in the healthy subjects. Am J Chin Med. 33(1), 2005, p. 157-64.
265) Vincent, C. and G. Lewith, Placebo controls for acupuncture studies. J R Soc Med. 88(4), 1995, p. 199-202.
266) Haker, E., Effect of sensory stimulation (acupuncture) on sympathetic and parasympathetic activities in healthy subjects. J Auton Nerv Syst. 79(1), 2000, p. 52-9.
267) Birch, S.H., R. Trinh, K. Zaslawski, C., The non-specific effects of acupuncture treatment: when and how to control for them. Clin Acupunct Orient Med. 3, 2002, p. 20-5.
268) Lund, I., J. Naslund, and T. Lundeberg, Minimal acupuncture is not a valid placebo control in randomised controlled trials of acupuncture: a physiologist's perspective. Chin Med. 4, 2009, p. 1.
269) Mayer, D.J., Acupuncture: an evidence-based review of the clinical literature. Annu Rev Med. 51, 2000, p. 49-63.
270) Haker, E. and T. Lundeberg, Laser treatment applied to acupuncture points in lateral humeral epicondylalgia. A double-blind study. Pain. 43(2), 1990, p. 243-7.
271) Gottschling, S., et al., Laser acupuncture in children with headache: a double-blind, randomized, bicenter, placebo-controlled trial. Pain. 137(2), 2008, p. 405-12.
272) Longhurst, J., The ancient art of acupuncture meets modern cardiology. Cerebrum: the Dana Forum on brain science. 3(4), 2001, p. 48-59.
273) Li, P., et al., Effect of electroacupuncture on pressor reflex during gastric

distension. Am J Physiol Regul Integr Comp Physiol. 283(6), 2002, p. R1335-45.
274) Zhou, W., et al., Afferent mechanisms underlying stimulation modality-related modulation of acupuncture-related cardiovascular responses. J Appl Physiol. 98(3), 2005, p. 872-80.
275) Longhurst, J., Acupuncture's beneficial effects on the cardiovascular system. Preventive Cardiology 21-33, 1998, p. 21-33.
276) Porkert, M.H., C.-H., Classical acupuncture. The standard textbook. 1995, Dinkelscherben: Phainon.
277) Hu, X., The normalization phenomenon of acupuncture on abnormal blood pressure, and some related observations . Shanghai Science and Technology (32), 1960.
278) Li, P.Y., T, Mechanism of the Modulatory Effect of Acupuncture on Abnormal Cardiovascular Functions . Shanghai Medical University Press . 13,32,41, 1992.
279) Whittaker, P., Laser acupuncture: past, present, and future. Lasers Med Sci. 19(2), 2004, p. 69-80.
280) Yao, T., S. Andersson, and P. Thoren, Long-lasting cardiovascular depression induced by acupuncture-like stimulation of the sciatic nerve in unanaesthetized spontaneously hypertensive rats. Brain Res. 240(1), 1982, p. 77-85.
281) Ernst, E.W., A., Acupuncture: a scientific appraisal. 1999: Butterworth Heinemann.
282) Filshie, J.C., M. , Western medical acupuncture , in Acupuncture: A Scientific Appraisal , E.W. Ernst, A. , Editor. 1999, Oxford: Butterworth-Heinemann . p. 31-59.
283) National Collaborating Centre for Primary Care. NICE clinical guideline 88: Low back pain Early management of persistent non-specific low back pain. 2009 1 June 2009 Available from: www.nice.org.uk/CG88.
284) Witt, C.M., et al., Treatment of the adverse effects from acupuncture and their economic impact: A prospective study in 73,406 patients with low back or neck pain. Eur J Pain.
285) Rapson, L.M., Acupuncture and adverse effects. Can Fam Physician. 49, 2003, p. 1588-9; author reply 1589, 1591.
286) Chung, A., L. Bui, and E. Mills, Adverse effects of acupuncture. Which are clinically significant? Can Fam Physician. 49, 2003, p. 985-9.
287) Ernst, G., H. Strzyz, and H. Hagmeister, Incidence of adverse effects during acupuncture therapy-a multicentre survey. Complement Ther Med. 11(2), 2003, p.

93-7.
288) Norheim, A.J., Adverse effects of acupuncture: a study of the literature for the years 1981-1994. J Altern Complement Med. 2(2), 1996, p. 291-7.
289) Omura, Y., Electrical parameters for safe and effective electro-acupuncture and transcutaneous electrical stimulation: threshold potentials for tingling, muscle contraction and pain; and how to prevent adverse effects of electro-therapy. Part 1. Acupunct Electrother Res. 10(4), 1985, p. 335-7.
290) Maciocia, G. (1994). The Practice of Chinese Medicine: The Treatment of Diseases with Acupuncture and Chinese Herbs (1 ed.). Edinburgh, UK: Churchill Livingstone.
291) Maciocia, G. (2005). The Foundations of Chinese Medicine: a comprehesive text for acupuncturist and herbalists (2 ed.). Oxford, UK & Philadelphia, MA, USA: Elsevier Churchill Livingstone.
292) Ni, M. (1995). The Yellow Emperor's Classic of Medicine: a new translation of the Neijing Suwen with commentary (1 ed.). Boston, Massachusetts, USA: Shambhala Publications, Inc.
293) Unschuld, P. U. (2003). Huang Di Nei Jing Su Wen: Nature, Knowledge, Imagery in an Ancient Chinese Medical Text (1 ed.). Berkeley, CA: University of California Press.
294) Hochberg, M. C., Altman, R. D., Brandt, K. D., Clark, B. M., Dieppe, P. A., Griffin, M. R., et al. (1995). Guidelines for the medical management of osteoarthritis. Part II. Osteoarthritis of the knee. American College of Rheumatology. Arthritis & Rheumatism, 38(11), 1541-1546.
295) White, A. (2006). Osteoarthritis of the knee -- an introduction. Acupuncture in Medicine, 24(Supplement), 1-6.
296) Zhang, B. Y., Dong, J. H., & Zhou, Z. Y. (1985). The Internal Medicine of Traditional Chinese Medicine (Chinese edition) (1 ed.). Shanghai, China: Shanghai Science & Technology Press.
297) Aung, S. K. H., & Chen, W. P. D. (2006). Clinical Introduction to Medical Acupuncture (1 ed.). New York, USA: Thieme Medical Publishers. Inc.
298) Felson, D. T., Lawrence, R. C., Hochberg, M. C., McAlindon, T., Dieppe, P. A., Minor, M. A., et al. (2000b). Osteoarthritis: New Insights Part 2: Treatment Approaches. Annals of Internal Medicine, 133(9), 726-737.
299) China State Administration of Traditional Chinese Medicine. (1994). Criteria of Diagnosis and Therapeutic Effect of Disease and Syndromes in Traditional

Chinese Medicine. Nanjing, China: Nanjing University Press.
300) China State Bureau of Technical Supervision. (1997). Clinic Terminology of Traditional Chinese Medical Diagnosis and Treatment -- Syndromes (1 ed.). Beijing, China: Standards Press of China.
301) Xiao, L. R. (2004). Formation of the Differentiation Theory and Treatment Principle of the Bi Syndrome of Bone (Osteoarthritis) During Qin, Han and Sui Dynasties. Journal of Fujian College of TCM, 14(2), 43-45.
302) Jiang, R. X., Wang, Y. Q., & Wang, H. Z. (2001). Treatment of Osteoarthritis in Chinese Medicine. Journal of Chengdu University of TCM, 24(4), 11-13.
303) Li, G. (2003). Prospective Survey of Osteoarthritis Research in Traditional Chinese Medicine (article in Chinese). Journal of Anhui TCM College, 22(6), 56-58.
304) Kwon, Y. D., Pittler, M. H., & Ernst, E. (2006). Acupuncture for peripheral joint osteoarthritis: A systematic review and meta-analysis. Rheumatology (Oxford), 45(11), 1331-1337.
305) White, A., Foster, N., Cummings, M., & Barlas, P. (2007a). Acupuncture treatment for chronic knee pain: a systematic review. Rheumatology (Oxford), 46(3), 384-390.
306) Lao, J. X., & Deng, C. (2003). Clinical observation on the treatment of genual osteoarthritis by electoacupuncture and moxibustion plus Chinese medicine (article in Chinese). Shanghai Journal of Acupuncture and Moxibustion, 22(8), 26-27.
307) Li, J. W., Xiang, S. Y., Ma, Z. Y., Feng, Y. B., Tong, H. Y., Geng, H. P., et al. (2008a). Clinical observation on cake-separated mild-warm moxibustion for treatment of knee osteoarthritis (article in Chinese). Chinese Acupuncture and Moxibustion, 28(1), 17-19.
308) Wu, S. (1998). Acupuncture in the treatment of knee osteoarthritis for 35 cases (article in Chinese). New Journal of Traditional Chinese Medicine, 30(2), 30-31.
309) Wu, Z. H., & Bao, F. (2008). Observation on therapeutic effects of electroacupuncture for the treatment of knee osteoarthritis (article in Chinese). China Journal of Orthopaedics and Traumatology, 21(3), 170-172.
310) Cai, Y. M., & Huang, W. Y. (2004). Observation of comparing three therapeutic methods on the treatment of knee osteoarthritis (article in Chinese). Shanghai Journal of Acupuncture and Moxibustion, 23(11), 22-23.
311) Lin, L. F., & Liang, Y. P. (2005). Clinical observation on electric needle therapy for

treatment of gonarthritis (article in Chinese). Chinese Acupuncture and Moxibustion, 25(10), 689-690.
312) Wang, J. G., & He, L. J. (2007b). Observation on the therapeutic effect of warming needle moxibustion on the knee osteoathritis (article in Chinese). Chinese Acupuncture and Moxibustion, 27(3), 191-192.
313) Bao, F., Wang, H. J., & Wu, Z. H. (2007). Current situation of acupuncture-moxibustion therapy on osteoarthritis and possible principle review (article in Chinese). Chinese Journal of Rehabilitation Theory and Practice, 13(4), 357-359.
Berman, B. M., Lao, L., Langenberg, P., Lee, W. L., Gilpin, A. M. K., & Hochberg, M. C. (2004). Effectiveness of acupuncture as adjunctive therapy in osteoarthritis of the knee: a randomized, controlled trial. Annals of Internal Medicine, 141(12), 901-910.
314) Lao, J. X., & Deng, C. (2003). Clinical observation on the treatment of genual osteoarthritis by electoacupuncture and moxibustion plus Chinese medicine (article in Chinese). Shanghai Journal of Acupuncture and Moxibustion, 22(8), 26-27.
315) Le, X. Y. (2001). Clinical observation on DAJ multi-function moxibustion apparatus for treatment of knee joint osteoarthritis (article in Chinese). Chinese Acupuncture and Moxibustion, 21(11), 687-688.
316) Li, C. D., Huang, X. Y., Yang, X. G., Wang, Q. F., & Huang, S. Q. (2006). Observation on therapeutic effect of warming needle moxibustion on knee osteoarthritis of deficiency-cold type (article in Chinese). Chinese Acupuncture and Moxibustion, 26(3), 189-191.
317) Lin, G. H., Li, W. Y., Su, G. L., & Zhong, B. M. (2004). Treatment of gonitis by warming needling: an observation of 40 cases (article in Chinese). New Journal of Traditional Chinese Medicine, 36(10), 48-49.
318) Wu, S. J., Wang, J., & Cao, J. C. (2006a). Illumination of External Application of Traditional Chinese Medicine - Li Yue Pian Wen (Proofread edition) (1 ed.). Beijing, China: People's Military Medical Press.
319) Yang, L. P., Wang, M. C., Liu, W. G., & Wang, M. Q. (2007). Effects of warming-needle therapy on gene expression pathways in the patient with knee osteoarthritis of deficiency-cold syndrome (article in Chinese). Chinese Acupuncture and Moxibustion, 27(9), 677-680.
320) Xi, M. J., Zhao, L., Shen, X. Y., Ding, G. H., Gao, J. P., Wang, L. Z., et al. (2008). Efficacy and specificity of laser acupuncture on the treatment of knee

osteoarthritis (article in Chinese). Journal of Clinical Rehabilitative Tissue Engineering Research, 12(26), 5075-5078.

321) Cao, Y. L., Pang, J., Wang, X., Shi, Y., Shen, W. D., Zheng, Y. X., et al. (2006). Current Status of Chinese Herbal Therapy for Osteoarthritis (article in Chinese). Chinese Journal of Clinical Rehabilitation, 10(35), 130-134.

322) Shi, Y. Y., Xu, S. R., & Chen, Y. H. (1994). Clinical Trial of Yang Xue Ruan Jian Formula in Treatment of Osteoarthritis (article in Chinese). Chinese Journal of Traditional Medicine Traumatology and Orthopedics, 2(4), 33-36.

323) Crepaldi, G., & Punzi, L. (2003). Aging and osteoarthritis. Aging Clinical and Experimental Research, 15(5), 355-358.

324) Guo, J. G., & Li, L. Y. (2003). Discussion on the Pathogenesis and Therapeutical Principle of Osteoarthritis (article in Chinese). New Journal of Traditional Chinese Medicine, 35(4), 3-5.

325) Birrell, F. N. (2004). Patterns of joint pain: lessons from epidemiology. Rheumatology (Oxford), 43(4), 408-409.

326) Herman, P. M., Craig, B. M., & Caspi, O. (2005). Is complementary and alternative medicine (CAM) cost-effective? A systematic review. BMC Complementary and Alternative Medicine, 5, 11-25.

327) Segal, L., Day, S. E., Chapman, A. B., & Osborne, R. H. (2004). Can we reduce disease burden from osteoarthritis? The Medical Journal of Australia, 180(5 Supplement), s11-s17.

328) Berman, B. M., Singh, B. B., Lao, L., Langenberg, P., Li, H., Hadhazy, V., et al. (1999). A randomized trial of acupuncture as an adjunctive therapy in osteoarthritis of the knee. Rheumatology (Oxford), 38(4), 346-354.

329) Manheimer, E., Linde, K., Lao, L., Bouter, L. M., & Berman, B. M. (2007). Meta-analysis: Acupuncture for Osteoarthritis of the Knee. Annals of Internal Medicine, 146(12), 868-877.

330) Witt, C., Brinkhaus, B., Jena, S., Linde, K., Streng, A., Wagenpfeil, S., et al. (2005). Acupuncture in patients with osteoarthritis of the knee: a randomised trial. Lancet, 366(9480), 136-143.

DECLARAÇÃO DE CONSENTIMENTO Considerando a “Declaração de Helsínquia” da Associação Médica Mundial (Helsínquia 1964; Tóquio 1975; Veneza 1983; Hong Kong 1989; Somerset 1996 e Edimburgo 2000)

Designação do estudo:

Explicação do estudo: A presente investigação, com base em ensaios clínicos, procurará determinar a influência da acupuntura no tratamento da rhizarthrosis e a sua eficácia enquanto técnica no âmbito da Tese de Mestrado de Medicina Tradicional Chinesa a decorrer no Instituto de Ciências Biomédicas Abel Salazar, Universidade do Porto.

The study will consist of one intervention group that will undergo 4 acupuncture treatments and one waiting list control group that will receive no intervention. The study being randomised subjects can be part of either group.

O projeto envolve acupunctura, quais os eventuais riscos envolvidos são a responsabilização da Escola de Heidelberg por eventuais danos.

A introdução de agulhas poderá causar um leve desconforto (sentido por algumas pessoas) no momento da picada, semelhante a uma agulha de injeção subcutânea.

Condições e financiamento: Os custos do estudo serão suportados inteiramente pelo investigador principal. Todos os dados e informações respeitantes aos participantes, serão sigilosas, e não poderão ser usados com outro propósito senão o de realização deste trabalho de investigação.

Eu, abaixo-assinado, _____(nome completo do doente),

compreendi a explicação que me foi fornecida acerca do meu caso clínico e da investigação que se tenciona realizar, bem como do estudo em que serei incluído. Foi-me dada oportunidade de fazer as perguntas que julguei necessárias, e de todas obtive resposta satisfatória. Tomei conhecimento de que, de acordo com as recomendações da

Declaração de Helsínquia, a informação ou explicação que me foi prestada versus os objectivos, os métodos, os benefícios previstos, os riscos potenciais e o eventual desconforto.

Além disso, foi-me afirmado que tenho o direito de recusar a todo o tempo a minha participação no estudo, sem que isso possa ter como efeito qualquer prejuízo na assistência que me é prestada. Por isso, consinto que me seja aplicado o método, o tratamento ou o inquérito proposto pelos investigadores.

Data: _____/_____/20__ Assinatura do paciente:

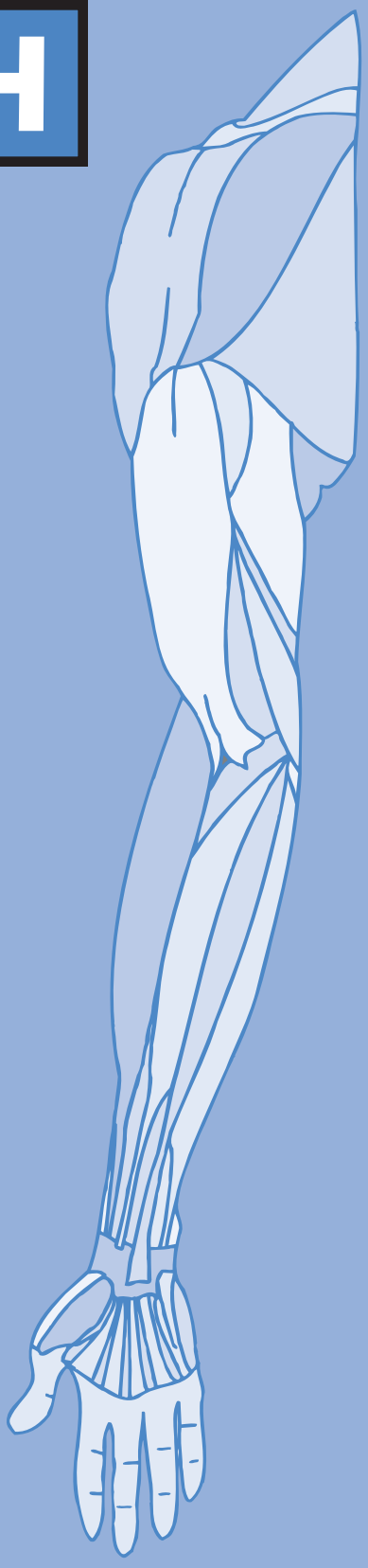
_____

Os investigadores responsáveis:

Nome: Christiane Grünecker

Nome: Nuno Correio

THE DASH



INSTRUCTIONS

This questionnaire asks about your symptoms as well as your ability to perform certain activities.

Please answer *every question*, based on your condition in the last week, by circling the appropriate number.

If you did not have the opportunity to perform an activity in the past week, please make your *best estimate* on which response would be the most accurate.

It doesn't matter which hand or arm you use to perform the activity; please answer based on your ability regardless of how you perform the task.

Disabilities of the Arm, Shoulder and Hand

Please rate your ability to do the following activities in the last week by circling the number below the appropriate response.

	NO DIFFICULTY	MILD DIFFICULTY	MODERATE DIFFICULTY	SEVERE DIFFICULTY	UNABLE
1. Open a tight or new jar.	1	2	3	4	5
2. Write.	1	2	3	4	5
3. Turn a key.	1	2	3	4	5
4. Prepare a meal.	1	2	3	4	5
5. Push open a heavy door.	1	2	3	4	5
6. Place an object on a shelf above your head.	1	2	3	4	5
7. Do heavy household chores (e.g., wash walls, wash floors).	1	2	3	4	5
8. Garden or do yard work.	1	2	3	4	5
9. Make a bed.	1	2	3	4	5
10. Carry a shopping bag or briefcase.	1	2	3	4	5
11. Carry a heavy object (over 10 lbs).	1	2	3	4	5
12. Change a lightbulb overhead.	1	2	3	4	5
13. Wash or blow dry your hair.	1	2	3	4	5
14. Wash your back.	1	2	3	4	5
15. Put on a pullover sweater.	1	2	3	4	5
16. Use a knife to cut food.	1	2	3	4	5
17. Recreational activities which require little effort (e.g., cardplaying, knitting, etc.).	1	2	3	4	5
18. Recreational activities in which you take some force or impact through your arm, shoulder or hand (e.g., golf, hammering, tennis, etc.).	1	2	3	4	5
19. Recreational activities in which you move your arm freely (e.g., playing frisbee, badminton, etc.).	1	2	3	4	5
20. Manage transportation needs (getting from one place to another).	1	2	3	4	5
21. Sexual activities.	1	2	3	4	5

Disabilities of the Arm, Shoulder and Hand

	NOT AT ALL	SLIGHTLY	MODERATELY	QUITE A BIT	EXTREMELY
22. During the past week, *to what extent* has your arm, shoulder or hand problem interfered with your normal social activities with family, friends, neighbours or groups? *(circle number)*	1	2	3	4	5

	NOT LIMITED AT ALL	SLIGHTLY LIMITED	MODERATELY LIMITED	VERY LIMITED	UNABLE
23. During the past week, were you limited in your work or other regular daily activities as a result of your arm, shoulder or hand problem? *(circle number)*	1	2	3	4	5

Please rate the severity of the following symptoms in the last week. *(circle number)*

	NONE	MILD	MODERATE	SEVERE	EXTREME
24. Arm, shoulder or hand pain.	1	2	3	4	5
25. Arm, shoulder or hand pain when you performed any specific activity.	1	2	3	4	5
26. Tingling (pins and needles) in your arm, shoulder or hand.	1	2	3	4	5
27. Weakness in your arm, shoulder or hand.	1	2	3	4	5
28. Stiffness in your arm, shoulder or hand.	1	2	3	4	5

	NO DIFFICULTY	MILD DIFFICULTY	MODERATE DIFFICULTY	SEVERE DIFFICULTY	SO MUCH DIFFICULTY THAT I CAN'T SLEEP
29. During the past week, how much difficulty have you had sleeping because of the pain in your arm, shoulder or hand? *(circle number)*	1	2	3	4	5

	STRONGLY DISAGREE	DISAGREE	NEITHER AGREE NOR DISAGREE	AGREE	STRONGLY AGREE
30. I feel less capable, less confident or less useful because of my arm, shoulder or hand problem. *(circle number)*	1	2	3	4	5

DASH DISABILITY/SYMPTOM SCORE = $\left[\left(\frac{\text{sum of n responses}}{n}\right) - 1\right] \times 25$, where n is equal to the number of completed responses.

A DASH score may <u>not</u> be calculated if there are greater than 3 missing items.